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The Arthur E. Mills Memorial Oration.[1]

ENGINEERING AND MEDICINE.

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IT is not difficult to find many similarities between the two great professions of medicine and of engineering. Both are essentially concerned with the improvement of man's control over his environment so that he may live a fuller, a healthier and possibly a longer life. Engineers, to be sure, are for the most part employed in dealing with inorganic problems, while the doctor's work is inherently organic in character, but this is a difference of detail rather than of principle. The similarities are much more significant, and in the course of this address I hope to touch on some of them and to try to draw from them conclusions which may have some educational significance.

There can be no doubt that both professions have their origin in the struggle for survival that has always been the dominant force in a man's life, and which drives the Melbourne business man to his office every day just as it drove the aborigines to hunt and fish. Primitive man had not advanced very far before he began to learn how to control fire, to make tools and to build shelters—to engage, indeed, in engineering activities of a simple kind. In the same way he began to learn, by hard experience, how to protect his body against poisons, wounds and burns, and how to help it to heal when it was damaged or diseased. The failures, no doubt, were for thousands of years only slightly less significant than the successes, but we should not be here tonight, in comparative safety and comfort, if the balance had not been on the credit side.

For almost all of man's history, certainly until the last few hundred years, his command of engineering technique and his knowledge of medicine were entirely empirical, being based on direct observation of the results of previous action. Here engineering had a great advantage, for it is much easier to discover how to construct bridges and buildings, how to convey water, how to plough and reap, spin and weave, than it is to observe what previous cause makes a man fall ill and die. Moreover, man's preoccupation with his own consciousness stood—and still stands—in the way of his realization that cause and effect were no less related within his own body than in the outer world that surrounds it.

[1] Delivered on May 25, 1960, at the Annual Ceremony of The Royal Australasian College of Physicians in the Wilson Hall, University of Melbourne.

This empirical growth of technical and medical knowledge is still going on, although it has been greatly modified and accelerated by discoveries in pure science and especially by the discovery of the scientific method. But it remains true that the activating motive of the pure scientist is quite different from that of the engineer or doctor. The scientist is essentially preoccupied with understanding the laws of nature and is not concerned, in principle at least, with any possible application of that knowledge. It was only the other day, for example, that we saw the first artificial satellite flying through the sky and demonstrating, for all to see, that the astronomers, from Galileo onwards, have been working on correct lines. (Incidentally, the fact that we do not know whether to regard this event as a triumph or as a tragedy is a regrettable indication that man's knowledge of the physical world far outstrips his knowledge of himself as a social animal.) Many other examples could be quoted of a similar kind: the nuclear reactor, radar and television, plastics, jet aircraft engines — all are examples of the exploitation of natural laws that were known to be true long before they could be used in practice. These are all examples from the physical world, with which we are mainly concerned tonight, but the same is true of the shadowy and insubstantial world of mathematics which is entirely a product of man's imagination. It occurred to George Boole, for instance, to examine the consequences of supposing, in effect, that there were only two numbers, 0 and 1; on this slender foundation he built a system of algebra, never for a moment imagining that it would later prove to be the basis on which electronic computers would be made to work.

The scientist, then, is an explorer of the physical world. Like Sir Edmund Hillary, who climbed Everest just because it was there, he is activated by curiosity, by the desire to understand what makes things happen as they do.

The doctor and the engineer, however, have the harder task of solving the problems that Nature presents in advance, very often, of a full understanding of all the natural laws that may be involved. No doctor would decline to treat a patient because the disease with which he was confronted was imperfectly understood or difficult to identify with certainty; no engineer would refuse to build a skyscraper because the steel might contain unsuspected flaws or even because the theory of the action of columns and beams was still incomplete. Both go as far as they can on the basis of established knowledge, but thereafter they have to fall back on empirical methods and, in the last resort, to rely on judgement and experience. In neither case, fortunately, does the public realize what is going on. Doctors, no less than anyone else, travel in aeroplanes, ride over bridges and switch on their radios, happily unaware of the guesses and half-truths on which they are relying, while the sick engineer gets into his hospital bed with as much confidence as the next man that he is already half-way to recovery.

This picture is, of course, oversimplified in these days of clinical research and engineering or applied science. It is probably true that at the present time most research is in fact directed to specific ends and that the pure scientist, *par excellence*, is now a comparatively rare figure; it is now only in the ivory towers of C.S.I.R.O., and perhaps in some universities, that he is able, lonely and disinterested, to engage in the pursuit of knowledge for its own sake. But it remains true that, although the detailed work of the researcher has in many cases become more like that of the practitioner, his motives and his whole mental approach to his work are still quite distinct.

This is at least very true of engineers and engineering research, and I suspect that it is equally true in your own field, although your account of the situation might appear, superficially, to be quite different from mine. I draw a clear distinction between design and analysis. Let us suppose that a civil engineer is required to carry a road across some obstacle; whether it be a small river or the English Channel does not matter, for the steps are the same, and the first one is always to imagine the possible solutions. The alternatives are obviously a bridge or a tunnel, but what kind of bridge will best suit the conditions? Is a tunnel practicable at all? At this stage the designer's mind is ranging freely over all sorts of possibilities, but gradually, as he collects information about the circumstances of the particular task, his ideas begin to be restricted until eventually he finds himself reduced to a close study of a small number of schemes, all variants, perhaps, of the one possibility that now seems to be open to him. During this process he will need information about the nature of the ground on the river banks and under its bed; about the road traffic his structure will have to carry in the immediate and in the more distant future; about the river traffic if any; about the levels and gradients on either side of the river where his approach works must be built; about flood levels and stream velocities and so forth. Some of this information will be readily available; some may require detailed investigation; some may even set in train elaborate studies which may require, or reveal, quite fundamental information. He must certainly consider how his structure is to be built; whether temporary support is practicable or permissible; whether this technique or that is in fact available to him because of local circumstances; whether long life and low maintenance are more or less important than first cost.

At this stage your profession and his may come very close together, as in Ghana, where the possible effect of a hydroelectric scheme on the incidence of water-borne disease had to be studied; or in Malaya, where the Perak River Dam could be built only after one of the first attempts at mosquito control was successful in preventing even a single case of malaria.

Finally, the engineer's thoughts culminate in a sketch design, and he is able to make to his client firm proposals on which a decision to proceed may be taken. It is only then that the analysis proper can be started and the detailed drawings, on which construction will later be based, put in hand. Once again problems will arise to which a solution must be found, but now, in all probability, time is more pressing and leisurely research is out of the question. The engineer's skill and judgement are likely to be very much in demand, but, of course, as knowledge and experience accumulate, the regions of uncertainty diminish, and yesterday's marvel becomes tomorrow's commonplace.

You will be able to judge, much better than I, how my hasty description of the progress of an engineering job corresponds with the way in which a doctor deals with a case of disease. But I am persuaded that the connected processes of diagnosis and treatment, whether medical or surgical, are quite analogous to the processes of design and construction. Imagination, investigation, the collection of information, the synthesis of a policy, the knowledge of techniques and the sheer technical skill, the exercise of judgement and the ability to work against time are required of doctor and engineer alike. At one point only is there a clear distinction: the physician relies on the skill of his hands perhaps rather less than the surgeon, but in this respect they are both quite different from the engineer, who has nowadays delegated manual dexterity to his craftsmen and, more and more, to his machines.

In another respect, however, the two professions have independently developed along very similar lines. In general terms the work of both is directed, as I have tried to show, to improving the physical lot of mankind, but in the particular case it is an individual client or patient who seeks advice and help. The fact that an engineer's client is often a company or a local council or even the government of a State does not disturb my argument, for then he has to deal with a group of laymen who are, collectively, just as ignorant of his craft as the individual patient is of the doctor's. The point is that unskilled people must, from time to time, employ the services of specialists in circumstances which prohibit, or at least severely restrict, the possibility of applying independent checks to their work; in short, the specialist has to be trusted. There

has thus grown up the conception of a professional relationship between doctor and patient, between engineer and client, which is in practice far more effective in ensuring that the vulnerable party is protected against exploitation than are the legal restraints that operate on commercial transactions. It is true that the law has introduced restraints at various points, especially in regard to medical practice, but these have for the most part only strengthened restraints that the profession had evolved for itself. By far the most powerful principle that applies to engineer and doctor alike is the moral one that requires him to identify his client's interest with his own, and this is indeed difficult to define in legal terms. It is, however, usually quite easy for informed colleagues to recognize when this principle has been betrayed, and for this reason society is, for the most part, ready to leave control of the whole matter in the hands of the profession itself.

This has led to the dual functions which the learned engineering societies now perform. On the one hand they continue, as they started, to promote by meeting and by publication the exchange of information between practitioners, and on the other they control admission to the profession by regulating training and conducting examinations. On occasion they exercise the judicial function and impose sanctions when they have determined that unprofessional conduct has occurred. The final step of clothing these processes in legal form is one that has only seldom been taken in the engineering field, perhaps for the reason that it is not always easy to ensure that it is the client and not his engineer who benefits the most.

It is perhaps rather surprising that there should be such a close correspondence between the outlook and methods of the two professions when the details of their work are usually so far apart. But there is, in fact, an increasing number of direct points of contact and of mutual interest. You will all think at once, no doubt, of the technical devices that are being used more and more in medical practice and whose origins lie elsewhere. Mechanical and electrical contraptions of continually increasing complexity are being pressed into service, for producing heat and cold, pressure or suction, and infra-red, ultra-violet and gamma radiation, and for measuring the most remote and secret phenomena of which the human body is capable. Indeed I am sometimes inclined to think that a new branch of engineering is in process of formation. Perhaps this new division of our profession, when really established, will be able to carry out the traditional role of the engineer and reduce the price while improving the performance of much of this medical machinery.

But I was rather thinking of such fields as industrial medicine and social and preventive medicine, where engineers and doctors are increasingly working in partnership. It is, of course, a commonplace that a pure and ample water supply and an adequate and reliable system of sewage disposal are the first essentials of public health, but there are many other ways in which modern industrial city life is developing so as to bring the two professions closer together. Very often it is the doctor who recognizes the danger and presses the engineer to avoid it. Thus the whole range of the various Factory Acts springs from the realization by medical men of the dangers inherent in technical operations, and, in our own day, the movement for smoke abatement gives expression to the growing belief that a polluted atmosphere is only less dangerous than a polluted water supply.

The study of man and machine in combination, however, is a development which has been brought to public notice quite recently in a very vivid way because the possibility of space travel is being so much discussed. Now that the technical problem of putting a satellite into orbit has been solved, it is evident that it would be quite possible to put a man into orbit too, and it might even be possible to bring him back to earth again. But the popular Press has made everyone realize that to keep a man alive and conscious in an entirely artificial environment is exceedingly difficult, quite apart from the problem of protecting him from the effects of acceleration and temperature necessarily involved in getting him off the earth in the first place. The elaborate experiments that have been carried out in order to study these medical problems of space travel are only the latest in the now well-established field of aviation medicine. This new specialty is usually thought of as dating from the last war, when "G-suits" were developed to prevent pilots of high-speed aircraft from blacking-out in turns or when pulling out of dives; but it is more instructive to think of it as being based on the studies of applied physiology which became necessary when technological advances required men to live and work in conditions to which their bodies were not well adapted. From this point of view the study of the disease known as "divers' bends", or even of the prevention of scurvy during long voyages, is part of the same discipline.

In another field the atomic bomb focused attention on the need to protect mankind from radiation hazards, and here, as elsewhere, information that sprang from military necessity found application in civilian life. The safe use of nuclear reactors, of radioactive isotopes and even of X-ray machines in shoe shops depends on research on the effects of radiation that was begun during the war and has continued ever since. The controversy over the possible dangers from radioactive fall-out demonstrates for all to see that there is still much to be learnt.

For most of us the difficulties of space travel and the dangers of radiation are fairly remote, it is to be hoped, but the motor-car is a machine with which we are all in almost daily contact—in one way or another. It is indeed surprising that, although motor accidents are now responsible for so many deaths and injuries as to make them as serious as a major disease, the effort devoted to finding their cause and minimizing their effects is still much less than that devoted to cancer, say, or tuberculosis. Here, one would have thought, was a fruitful field for collaborative work by doctors and engineers, but it was only in 1956 that the British Road Research Laboratory set up its crash investigation team. Their work, and that of other similar groups, has already demonstrated that the injuries sustained by the occupants of motor vehicles involved in accidents follow quite well defined patterns: injuries to the head and thorax, for example, are by far the most common, both in drivers and in passengers, while the injuries sustained by drivers are critically affected by the strength of the steering column. Information of this kind is already taking effect: crash helmets are now universally worn by motor cyclists in England, for example, and motorists everywhere are beginning to fit safety harness to their cars and, somewhat less frequently, to use it. The design of motor-car interiors has not yet been seriously considered from this standpoint, however, and the effect of motor-car exteriors on pedestrians is still, so far as I know, an almost unexplored subject. It is known, though, that if you have the misfortune to run over someone, it is wise to take the brakes off.

It remains true, unfortunately, that the contribution of doctors to the accident problem as a whole is remedial rather than preventive, but, as the efforts of engineers have so far been only partly effective, perhaps the time is ripe for the medical profession to intervene.

Consideration of the body and machines in combination leads naturally on to consideration of the body as a machine, or, at least, as a structure. To the best of my knowledge interest in the mechanism of movement of the body began with Leonardo da Vinci at the end of the fifteenth century. Since then, from time to time, there have been isolated attempts to apply mechanical principles to the study of the skeleton, in particular, both in a healthy and in a diseased or damaged state. Interest in this subject has, however, been growing recently, and last year the Institution of Mechanical Engineers in London arranged a symposium on what is now becoming known as biomechanics. The contributions to this symposium, from doctors and engineers, demonstrated very clearly that hardly anything was known about even quite fundamental matters such as the strength of bones or the lubrication of joints. Speaking as one who has frequently suffered

from lumbago, I hope that this state of affairs will be speedily improved.

It is indeed evident that biomechanics, undeveloped as it still is, has made practically no contribution to medical knowledge, certainly much less than biochemistry or biophysics. Why should this be? Is it that doctors have regarded it as being relevant only to orthopædic surgery, which I am given to believe is regarded as a not entirely respectable pursuit? Or is it that the medical student is compelled, at an early and vulnerable age, to take courses in physics and chemistry, and so to have at least a nodding acquaintance with those sciences while remaining completely ignorant of the engineering sciences? It may perhaps be that the latter have in fact less to offer to the medical man than the others, but one cannot be sure of this in the present state of knowledge.

The comparatively elementary work that is being done has at least the advantage that the literature is simple enough to be read with pleasure by the layman. D'Arcy Thompson's classic "On Growth and Form" is a fascinating introduction; there one can find all sorts of biological phenomena discussed in the light of engineering principles including, believe it or not, Lord Kelvin's discovery that small shaggy dogs keep cooler than large shaggy dogs.

More recently, Sir James Gray, of Cambridge, has devoted a lifetime to the study of how animals move. Starting from the analogy between a quadruped and a four-legged table, he shows that one of the things that happen if an animal lifts one leg is that its centre of gravity shifts until it is directly over the centre of pressure of the remaining three feet. From there it is an easy step to see that if it lifts a second leg it is extremely foolish, especially if both the raised legs are on the same side.

Returning to lumbago, we note that Hirsch, in Sweden, using instruments and techniques that are perfectly familiar to engineers, seems to have thrown considerable light on the mechanical behaviour of the intervertebral disks and on the changes in fluid pressure within them caused by external loads on the spine. While he freely admits that he has not yet completely explained lumbago, still less cured it, there is some satisfaction in knowing that science confirms that it is unwise to attempt to fasten one's shoe laces while carrying a heavy weight on one's head.

Mr. President, I promised at the beginning of this address to conclude by drawing some conclusions about medical, and perhaps engineering, education from this hasty sketch of some of the points of contact between the two professions. Now that I approach this part of my task, I find myself in a real difficulty, for the only valid conclusion I can draw is that both doctors and engineers have to know an awful lot. They are not unique in this, but the nature of their work puts them in a special difficulty; for it is not sufficient to cram more and more into courses of the present length or to increase the number of undergraduate or pre-clinical years. Indeed, this may be worse than useless unless care is taken to emphasize that the creative, synthetic application of scientific principles is the key to successful practice and that the mere acquisition of scientific knowledge is not, by itself, sufficient.

The organized clinical education of medical students in hospitals is, I have to admit, far superior to the corresponding graduate apprenticeship of the young engineer, and it gives a wonderful opportunity for the fledgeling doctor to develop the qualities I have tried to illustrate. But the challenge of advancing knowledge is felt most keenly, I am sure, in the first three or four years of university life; here there must surely be, on the one hand, the most ruthless pruning of irrelevant and outdated material and, on the other, the greatest possible correlation and integration of the different branches of science.

Above all, we must never forget the fact that doctor and engineer alike work with and for their fellow men; they must learn means but never lose sight of ends.

THE DILUTION ANÆMIA OF PREGNANCY.

By M. G. WHITESIDE, M.D., M.R.A.C.P.,

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THE main cause of a fall in hæmoglobin level during pregnancy has been shown to be iron deficiency (Benstead and Theobald, 1952; Fisher and Biggs, 1955; Edgar and Rice, 1956; Kerr and Davidson, 1958, and many others), and iron deficiency anæmia is sufficiently common to warrant routine administration of iron to all women during pregnancy. However, even when adequately treated with iron a small proportion of women still become anæmic. In most of these no cause is found for the anæmia on routine investigation, and no response is obtained with any available hæmatinic agent. An excessive rise in plasma volume, associated with a normal rise in red-cell volume, is thought by some to be the most likely explanation (Kerr and Davidson, 1958); but the studies on which this concept is based were done without regard for possible iron deficiency (Dieckmann and Wegner, 1934; Tysoe *et alii*, 1950; Caton *et alii*, 1951). Another explanation (Holly, 1953; Holly and Grund, 1959) is that the anæmia is the result of a failure of the bone marrow to increase its red-cell production commensurately with a normal increase in plasma volume. The variation among normal individuals in the degree of increase in both plasma and red-cell volume during pregnancy is so wide (Lund and Sisson, 1958) that the problem of deciding whether the abnormality lies in the plasma volume excess or the failure of the red-cell volume to keep pace with it is not an easy one. Certainly it is difficult to say whether the figures for an individual at any particular stage of pregnancy are normal or abnormal; but the answer to the problem should emerge from group studies.

This paper presents the results of a preliminary investigation to determine whether an excessive rise in plasma volume does occur in association with adequate iron treatment. Serial plasma protein estimations were made on all patients and have been found of value in assessing the results.

Materials and Methods.

Twenty-three pregnant women were selected for study early in pregnancy. The selection was random, without regard to their initial hæmoglobin level, though in all but four it was above 12 grammes per 100 ml. The plasma volume, red-cell volume and electrophoretic pattern of serum proteins were determined shortly after the patients' first visit to hospital, and these investigations were repeated, together with estimation of the serum iron level, at 28 to 33 weeks' gestation, the stage when anæmia usually becomes most severe. All women at their first visit were ordered 200 mg. of ferrous sulphate three times a day for the remainder of their pregnancy, and all maintained that they were taking it with reasonable regularity throughout the period of the study.

The plasma volume was measured by the use of the dye T-1824 (Evans blue). This has been shown not to enter the liquor or the fœtal circulation (Gibson and Evans, 1937), and the results obtained with it compare favourably with those from other methods (Strumia *et alii*, 1958). Venous blood was withdrawn without compression into a heparin tube for a "pre-dye" specimen of plasma, and into a Wintrobe oxalate tube for estimation of the hæmoglobin and hæmatocrit. A syringe containing approximately 5 ml. of a solution of the dye (5 mg. per ml.) was weighed, its contents were injected intravenously and the syringe was weighed again. An accurate measure of the amount of dye given was thereby obtained. Thirty minutes later a further sample of blood was withdrawn without compression into a heparin tube. The dye was extracted from the plasma in accordance with the method of Allen (1953).

Pre-dye and post-dye samples of plasma were treated in the same way, the final solution was compared in a

TABLE I.

Case Number.	Patient's Age. (Years.)	Gravidity.	Early in Pregnancy.					Late in Pregnancy.							
			Gestation. (Weeks.)	Hæmoglobin Value. (Grammes per 100 ml.)	Weight. (Kilograms.)	R/K.[1] (Millilitres.)	P/K.[2] (Millilitres.)	Gestation. (Weeks.)	Hæmoglobin Value. (Grammes per 100 ml.)	Serum Iron Content. (Microgrammes per 100 ml.)	Weight. (Kilograms.)	R/K.[1] (Millilitres.)	P/K.[2] (Millilitres.)	Change in R/K.	Change in P/K.
Group A.															
I	21	1	19	12·6	56·7	26·0	58·9	32	12·6	102	64·0	27·7	53·6	+7%	−9%
II	32	2	11	13·1	83·0	23·2	46·4	30	13·4	114	86·1	24·0	48·0	+3%	−3%
III	28	1	16	11·6	54·5	24·4	57·6	32	12·2	114	60·3	31·5	62·8	+29%	+9%
IV	27	1	8	13·0	64·0	21·9	49·4	31	12·7	85	76·7	21·5	48·7	−2%	−1%
V	23	3	13	10·4	49·0	28·6	70·5	32	12·3	91	56·3	27·2	63·7	−5%	−10%
VI	23	3	12	13·2	67·0	29·7	53·8	30	14·9	94	75·0	27·3	50·6	−8%	−6%
VII	21	2	9	12·4	55·4	27·2	53·7	30	12·5	82	65·4	24·7	61·2	−9%	+14%
VIII	27	4	9	11·8	64·4	26·7	58·2	28	12·8	107	68·6	28·7	62·3	+8%	+7%
IX	23	2	11	13·6	60·9	33·2	61·2	30	14·4	91	72·2	33·2	61·5	0%	0%
X	22	1	8	13·2	54·0	26·7	53·3	32	13·5	101	63·0	25·1	54·4	−6%	+2%
XI	23	3	8	13·6	60·3	31·8	59·0	33	14·4	137	72·8	30·5	60·9	−4%	+3%
XII	19	1	13	13·2	55·4	28·5	59·9	33	12·2	83	67·3	23·3	52·8	−18%	−12%
Means..	24	—	11	12·6	60·4	27·3	56·8	31	13·2	100	68·9	27·1	56·7	0%	0%
Group B.															
I	34	2	14	14·4	49·1	27·5	53·0	28	11·8	85	54·5	26·7	60·3	−3%	+13%
II	28	2	12	13·6	59·0	30·5	61·3	32	11·4	101	65·2	32·9	74·3	+8%	+21%
III	17	1	19	12·8	68·6	23·2	52·4	32	11·4	122	79·5	26·9	63·5	+16%	+21%
IV	31	3	8	14·4	51·2	28·3	52·2	32	11·4	191	58·0	24·5	62·6	−13%	+19%
V	24	2	14	12·8	58·5	22·1	46·9	31	11·4	288	66·8	22·7	52·7	+3%	+13%
VI	28	1	6	13·2	55·8	25·0	54·5	29	11·8	123	63·5	23·3	59·6	−7%	+9%
VII	34	7	12	13·0	54·9	26·7	55·9	30	11·1	108	62·6	30·7	78·3	+15%	+40%
VIII	29	2	8	12·6	46·0	26·3	52·6	30	11·6	85	52·2	26·4	59·4	0%	+13%
IX	30	6	8	11·4	56·7	19·7	43·0	29	11·1	87	60·8	23·6	63·3	+23%	+46%
X	30	2	11	12·2	66·8	23·7	49·4	33	11·4	86	73·0	26·0	64·4	+10%	+30%
XI	23	1	15	13·3	63·7	19·5	40·8	32	11·8	90	82·7	23·2	52·3	+19%	+28%
Means..	28	—	11	13·1	57·2	24·5	51·1	31	11·5	124	66·3	26·1	62·8	+6%	+23%

[1] Red-cell volume per kilogram of body weight.

[2] Plasma volume per kilogram of body weight.

Hilger "Spekka" photoelectric colorimeter[1] and the dye concentration was read from a standard curve. This figure was multiplied by 100/95 to obtain the concentration at zero time (Mollison, 1958), and the plasma volume was then calculated. The venous hæmatocrit was corrected for trapped plasma, converted to body hæmatocrit by the factor 0·91 (Mollison, 1956) and used for calculation of the red-cell volume.

Serum iron estimations were made by the method described by Powell (1944). The patients were told to take no iron tablet on the morning of the test, and blood specimens were all obtained at about 10 a.m. The total serum proteins were measured by the Kjeldahl method using steam distillation for nitrogen estimation. Non-protein nitrogen was calculated from the blood urea. The serum was then run on an E.E.L. electrophoresis apparatus,[2] the paper being stained with Azocarmine B and scanned on an E.E.L. scanner[2]. Corrections for the staining were applied in accordance with the method described by Crook *et alii* (1954). Hæmoglobin estimations were made by the oxyhæmoglobin method using an E.E.L. photoelectric colorimeter[2] calibrated regularly. Blood films were examined and total and differential white cell counts were made concurrently with each plasma volume measurement.

Results.

The plasma and red-cell volume findings are shown in Table I. Twelve patients showed no fall in hæmoglobin level late in pregnancy (Group A); but in the remaining 11, the hæmoglobin value fell below 12 grammes per 100 ml. despite normal serum iron levels (Group B). The weights and weight gains in the two groups were comparable. It can be seen that in Group A both the red-cell volume per kilogram of body weight (R/K) and the plasma volume per kilogram of body weight (P/K) remained fairly constant for individuals, though there was a wide variation within the group. The mean R/K and the mean P/K for the groups were not significantly different at the two stages of gestation; indeed, the similarity of the figures was remarkable. In this group, then, the red-cell volume and the plasma volume increased commensurately with the body weight, and anæmia did not occur.

In Group B, R/K similarly did not differ significantly between the two stages of gestation, and the figures were not significantly different from those of Group A. However, the mean P/K in this group rose by 23% and this increase was highly significant ($P < 0.001$). Comparison of the P/K figures for the two groups at the later stage of gestation showed that the differences were also probably significant ($0.05 > P > 0.02$). The studies of the peripheral blood did not reveal any cause for the anæmia in Group B, nor were the findings in any way different from those in Group A. The mild anæmia in Group B was therefore associated with an excessive rise in the plasma volume.

Table II summarizes the results of the serum protein measurements in the two groups. In Group A, the changes seen late in pregnancy were similar to those usually described for normal pregnancy—namely, a fall in total protein, albumin and gamma-globulin levels, with a rise in alpha-1, alpha-2 and beta globulin levels (Mack, 1955; Brown *et alii*, 1959). In Group B, the alpha-1 and alpha-2 globulin levels fell instead of rising, though the other changes were similar. Comparison of the

[1] Hilger and Watts Ltd., London.

[2] Evans Electroselenium Ltd., Harlow, Essex, England.

TABLE II.
Mean Serum Protein Levels.

Serum Protein Level. (Grammes per 100 ml.)	Group A.			Group B.		
	Early in Pregnancy.	Late in Pregnancy.	Change.	Early in Pregnancy.	Late in Pregnancy.	Change.
Total	6·5	6·0	−8%	6·46	5·89	−9%
Albumin	3·39	2·79	−18%	3·22	2·85	−12%
Alpha-1 globulin	0·39	0·40	+3%	0·41	0·35	−15%
Alpha-2 globulin	0·63	0·71	+13%	0·63	0·54	−14%
Beta globulin	0·81	1·02	+27%	0·85	0·98	+15%
Gamma globulin	1·28	1·09	−15%	1·36	1·17	−14%

figures for the two groups at the later stage of gestation showed that, though the difference between the alpha-1 globulin levels was not significant ($0{\cdot}4 > P > 0{\cdot}3$), the difference between the alpha-2 globulin levels was significant ($P < 0{\cdot}01$).

In the two groups the age and the gravidity of the patients were comparable.

Discussion.

The results in Group A show that normal pregnant women adequately treated with iron can maintain a constant hæmoglobin level during their pregnancy, and that, as Lund and Sisson (1958) have noted, the rise in red-cell and plasma volumes which occurs is usually proportional to their gain in weight. However, the results in Group B suggest that dilution anæmia can still occur in spite of adequate iron treatment. The large proportion of patients in this group raises the possibility that some at least may have been iron-deficient; but the evidence against this is strong. The serum iron levels in the group were all normal (although it is recognized that these estimations are not infallible), and iron-deficiency was not reflected in the red-cell volume figures, which were comparable with those of the non-anæmic patients in Group A.

An excessive rise in plasma volume is therefore regarded as the most likely cause for the anæmia in Group B; but before this is accepted, one other possible explanation should be considered. From the results of their blood volume studies, Lund and Sisson (1958) were able to group women during pregnancy into hypovolæmic, isovolæmic and hypervolæmic subjects. It is possible therefore that Group B consisted of naturally hypervolæmic subjects in whom the red-cell volume had failed to increase commensurately with the plasma volume owing to relative hypoplasia of the bone marrow. While the number of cases involved is too small to refute this suggestion of bone-marrow hypoplasia, it would appear at present to be an unlikely explanation of the anæmia. This raises the question why a rise in plasma volume can outstrip red-cell production. It is generally thought that the rise in plasma volume is the main stimulus to the marrow; but the increase in plasma volume is perhaps sometimes too rapid even for normal marrow to keep pace with it. On the other hand, it is possible that the red-cell volume is controlled by quite a different mechanism, and once it has reached an optimal size there is no further stimulus for its increase. This idea is supported by observations (unpublished) of the effects of blood transfusion on patients developing anæmia early in the third trimester, when the hæmoglobin level frequently returns to the pre-transfusion figure within a few weeks.

Finally, it is pertinent to inquire into the significance of this excessive rise in plasma volume. Study of a much larger series is necessary to decide whether or not it is associated with an increased incidence of obstetrical complications. However, that it occurs in a minority of patients (probably in less than the results in this series show) suggests that it is not physiological, and in support of this the serum protein findings are perhaps more significant. Not only did the electrophoretic pattern of the anæmic group differ from the non-anæmic group late in pregnancy, but the changes developing in the pattern in the anæmic group differed from those usually described for normal pregnancy. It is not proposed here to discuss further the significance of these findings; but it is suggested that the phenomenon of the dilution anæmia of pregnancy deserves more close scrutiny before it is accepted as physiological.

Summary.

Of 23 women receiving adequate iron treatment during pregnancy, 12 maintained a constant hæmoglobin level and the increase in total red-cell volume and total plasma volume were proportional to the gain in weight. In these 12, the changes in the protein pattern were similar to the changes reported for normal pregnancy.

In the remaining 11, a significant fall in hæmoglobin level was observed, the fall being associated with an excessive rise in plasma volume and a normal rise in red-cell volume. The serum protein changes in this group differed from the changes in the non-anæmic group and from those in normal pregnancy.

It is concluded that an excessive rise in plasma volume can be a cause of anæmia in pregnancy despite adequate iron treatment, and that this condition of dilution anæmia warrants further study.

Acknowledgements.

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References.

ALLEN, T. H. (1953), "Comparison of Plasma Volumes Measured by Direct Photometry and by Extraction of T-1824 in Dog and Man", *Amer. J. Physiol.*, 175: 227.

BENSTEAD, N., and THEOBALD, G. W. (1952), "Iron and the Physiological Anæmia of Pregnancy", *Brit. med. J.*, 1: 407.

BROWN, D. F., MCGANDY, R. B., GILLIE, E., and DOYLE, J. T. (1959), "Observations on Some Serum Components in Mothers and in their Newborn Infants", *Amer. J. Obstet. Gynec.*, 77: 556.

CATON, W. L., ROBY, C. C., REID, D. E., CASWELL, R., MALETSKOS, C. J., FLUHARTY, R. G., and GIBSON, J. G. (1951), "The Circulating Red Cell Volume and Body Hæmatocrit in Normal Pregnancy and the Puerperium", *Amer. J. Obstet. Gynec.*, 61: 1207.

CROOK, E. M., HARRIS, H., HASSAN, F., and WARREN, L. F. (1954), "Continuous Direct Photometry of Dyed Material in Filter Paper with Special Reference to the Estimation of Proteins Separated by Electrophoresis", *Biochem. J.*, 56: 434.

DIECKMANN, W. J., and WEGNER, C. R. (1934), "The Blood in Normal Pregnancy", *A.M.A. Arch. intern. Med.*, 53: 71.

EDGAR, W., and RICE, H. M., (1956), "Administration of Iron in Ante-Natal Clinics", *Lancet*, 1: 385.

FISHER, M., and BIGGS, R. (1955), "Iron Deficiency in Pregnancy", *Brit. med. J.*, 1: 385.

GIBSON, J. G., and EVANS, W. A. (1937), "Clinical Studies of the Blood Volume. 1. Clinical Application of a Method

Employing the Azo Dye Evans Blue and the Spectrophotometer", *J. clin. Invest.*, 16: 301.

HOLLY, R. G. (1953), "Hypoplastic Anæmia in Pregnancy", *Obstet. and Gynec.*, 1: 535.

HOLLY, R. G., and GRUND, W. J. (1959), "Ferrodynamics During Pregnancy", *Amer. J. Obstet. Gynec.*, 77: 731.

KERR, D. N. S., and DAVIDSON, S. (1958), "The Prophylaxis of Iron-Deficiency Anæmia in Pregnancy", *Lancet*, 2: 483.

LUND, C. J., and SISSON, T. R. C. (1958), "Blood Volume and Anæmia of Mother and Baby", *Amer. J. Obstet. Gynec.*, 76: 1013.

MACK, H. C. (1955), "The Plasma Proteins in Pregnancy", Thomas, Springfield.

MOLLISON, P. L. (1956), "Blood Transfusion in Clinical Medicine", Blackwell, Oxford.

POWELL, J. F. (1944), "Serum Iron in Health and Disease", *Quart. J. Med.*, 13: 19.

STRUMIA, M. M., COLWELL, L. S., and DUGAN, A. (1958), "The Measure of Erythropoiesis in Anæmias. 1. The Mixing Time and Immediate Post-Transfusion Disappearance of T-1824 Dye and of Cr^{51}-tagged Erythrocytes in Relation to Blood Volume Determination", *Blood*, 13: 128.

TYSOE, F. W., LOWENSTEIN, L., and SIMON, F. (1950), "Blood Volume and Hæmatological Studies in Pregnancy and the Puerperium", *Amer. J. Obstet. Gynec.*, 60: 1187.

A COMPARATIVE STUDY OF PREGNANCY AND LABOUR IN PRIMIPARÆ OF INCREASING AGE.

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DISCUSSIONS on the complications of pregnancy and labour in the elderly and the very young, with statistical support, have appeared in medical journals of overseas countries from time to time. It is proposed to examine these complications under local conditions and to compare four separate age groups spread throughout the fertile age range, with a view to determining at what age a primipara becomes elderly and to assess the risk involved.

The reduction in the incidence of preeclamptic toxæmia when ante-natal care is commenced before the sixteenth week of pregnancy has been shown by Stevenson (1953).

The fluctuations of blood pressure readings and their significance have been clearly stated by Brown and Brown (1955) and by Townsend (1959).

The writings of De Lee and Greenhill (1951), Dennen and Ainslie (1951), Fredrikson and Anberg (1956) and Points (1957) have indicated the increased incidence of ante-partum hæmorrhage, breech presentation and prematurity in the elderly primipara. Because of these complications, there is a greater need for obstetrical interference, and this increases with age.

It will be shown that, with the exception of preeclamptic toxæmia and some reduction in the duration of labour, the complications occurring in the elderly primipara have altered very little in the last ten years. However, it is suggested in this series that the age of the elderly primipara has risen to 37 years and over.

Material and Methods.

This paper considers 400 first pregnancies and labours occurring in patients whose ages ranged from 15 to 46 years. The histories are from The Women's Hospital, Crown Street, Sydney, and the selection of cases was made by age, parity and the continuation of pregnancy beyond the twenty-eighth week. For this study they are arranged in four groups. Each group contains the histories of 100 patients. A comparison is made between all groups of the following: (*a*) average blood pressure, (*b*) occurrence of preeclamptic toxæmia, (*c*) occurrence of ante-partum hæmorrhage, (*d*) duration of pregnancy, (*e*) length of first and second stages of labour, (*f*) occurrence of post-partum hæmorrhage, (*g*) outcome for the fœtus.

Statistical Results.

Average Blood Pressure.

First, consideration has been given to the blood-pressure readings of each group taken at the first visit before the sixteenth week of pregnancy. The number of patients concerned, together with the average of the readings of systolic and diastolic pressure, are set out in Table II. There was no difference with increasing age.

TABLE I.
Ages and Grouping.

Group.	Age (Years).	Number of Patients.
I	15 to 18	100
II	25 to 28	100
III	35 to 37	100
IV	38 and over	100

The reading of blood pressure obtained at the first visit in any case is given preference over the average of two or possibly three readings that may have been recorded before the sixteenth week of pregnancy. It is considered that the influence of an emotional factor, if it is present, will be at its highest on that occasion. Any subsequent reading of blood pressure higher than this initial one must be due to a pathological cause.

Hypertension.

Any series of blood-pressure readings when studied may be divided into three groups: (i) those that are considered normal and below normal; (ii) those that are accepted as hypertensive; (iii) an intermediate group about which there is diversity of opinion. In this series the standards of blood pressure adopted are as follows: (i) normal, 130/70 mm. of mercury or below; (ii) hypertensive, 140/85 mm. of mercury or above; (iii) potentially hypertensive, those readings falling between (i) and (ii). In addition, any patient whose diastolic blood pressure shows a sustained rise of 15 mm. of mercury or more is considered to be hypertensive, even though the actual reading does not reach the standard reading of 140/85 mm. of mercury accepted as hypertension in this paper.

TABLE II.
Average of Blood Pressure Readings Before the Sixteenth Week of Pregnancy.

Group.	Blood Pressure. (Millimetres of Mercury.)	Number of Patients.
I	129/71	51
II	128/70	77
III	133/71	77
IV	126/70	56

TABLE III.
Variation in Blood Pressure during Pregnancy in Patients Seen Before the Sixteenth Week.[1]

Group.	Essential Hypertension.	Potential Hypertension.	Hypertension Developed.	Pre-eclampsia.
I	2 (1)	19 (3)	2	4
II	1 (1)	30 (3)	3	5
III	11 (2)	32 (0)	7	4
IV	9 (1)	19 (2)	10	5

[1] The figures in parentheses indicate the essential or potential hypertensives who developed preeclamptic toxæmia.

The blood-pressure findings of those patients examined for the first time at or before the sixteenth week of pregnancy are shown in Table III.

As expected, there is a larger proportion of patients with essential hypertension in the older age group (15%) in comparison with the younger age group (2·4%). A larger proportion of older patients become more hypertensive or develop hypertension during pregnancy.

Those patients who develop classical signs of pre-eclamptic toxæmia are equally distributed throughout the age groups; this seems to be so regardless of the raised blood-pressure readings in the older age group. Those patients classified as potentially hypertensive, together with those classified as essentially hypertensive, give rise to the majority of cases of preeclamptic toxæmia in all age groups. In Table III the figures in parentheses indicate the essential or potential hypertensives who developed preeclamptic toxæmia.

In this series (all patients seen), the number of patients who developed hypertension increased greatly after the age of 37 years, but the number of patients who showed evidence of preeclamptic toxæmia remained the same (Table IV).

TABLE IV.
Hypertension and Preeclampsia in All Patients Seen.

Group.	Hypertension.	Pre-eclampsia.
I	2	9
II	4	5
III	8	8
IV	22	8

Ante-Partum Hæmorrhage.

Ante-partum hæmorrhage occurred in 11 cases in the present series; 10 of these patients were aged over 35 years when the hæmorrhage occurred. The causes of the hæmorrhage are set out in Table V.

TABLE V.
Causes of Ante-Partum Hæmorrhage.

Group.	Placenta Prævia.	Accidental Hæmorrhage.	Unknown.
I	0	0	1
II	0	0	0
III	1	1	1
IV	2	5	0

Three of the five patients with accidental hæmorrhage in Group IV were seen at the hospital for the first time with the condition present, and the remaining two patients were under ante-natal care before the sixteenth week of pregnancy.

Duration of Pregnancy.

In this series the expected duration of pregnancy in any given case has been calculated on the findings of Harvey Sutton (1945), plus or minus an allowance for menstrual irregularities.

The number of deliveries that occurred each week from 35 to 43 weeks' gestation are set out graphically in Figure I.

Identical distributions, with the peak at term plus seven days, are shown in Group I and Group II. The same type of distribution, but with the peak one week earlier — that is, at term — is shown in Group III. A completely different distribution pattern is shown in Group IV, with deliveries spread evenly over four weeks.

The actual numbers of completed deliveries and times are shown in Table VI.

Prolonged pregnancy was considered to have occurred in nine cases. In their subsequent labours, four babies showed evidence of distress, one of whom subsequently died from a cerebral hæmorrhage, considered to be due to anoxia caused by the prolongation of pregnancy.

Labour.

Spontaneous labour occurred most frequently Group I and least frequently in Group IV, as shown in Table VII.

The number of inductions of labour, either medical or surgical, rose with increasing age, as did the number of prolonged labours, prolonged labour being designated as such after 30 hours in the first stage (Ostry, 1955; Sturrock and Brown, 1956).

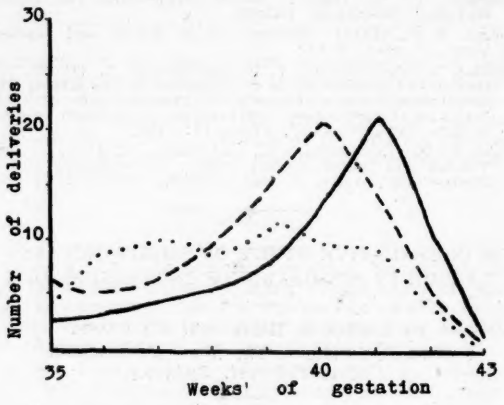

FIGURE I.
Distribution of deliveries from 35 to 43 weeks. Solid line, Groups I and II; interrupted line, Group III; dotted line, Group IV.

The average duration of the first and second stages of labour is set out in Table VIII.

The duration of the first stage of labour lengthens with increasing age; but at its maximum, in Group IV, it is still shorter in this series than in other published figures

TABLE VI.
Number of Deliveries at Term and Over.

Group.	Term.	Term Plus 7 Days.	Term Plus 14 Days.	Prolonged Pregnancy.
I	52	77	97	3
II	58	85	99	1
III	65	82	97	3
IV	70	84	98	2

(Fredrikson and Anberg, 1956). It is suggested that this has a direct bearing on the dietary factor involved, and on the general state of nutrition of the female population in this country.

TABLE VII.
Types of Labour with Number of Patients.

Group.	Spontaneous Labour.	Induced Labour.	Prolonged Labour.	No Labour.
I	95	5	5	0
II	90	10	9	0
III	87	12	16	1
IV	72	18	12	10

The duration of the second stage of labour in all age groups is short. In Groups III and IV this is directly attributed to the high forceps rate involved.

Cæsarean section was carried out without a trial of labour in 11 cases, and the indications are set out in Table IX.

The Method of Delivery.

The method of delivery and its immediate complications are set out in Table X.

The number of normal deliveries decreases with increasing age; this decrease is accompanied by a corresponding rise in the forceps rate.

TABLE VIII.
Average Duration of First and Second Stages of Labour.

Group.	First Stage. (Hours.)	Second Stage. (Hours.)
I	12·8	1·0
II	15·6	1·4
III	16·2	2·0
IV	19·2	1·8

There were 16 breech deliveries in all; two of these patients were delivered by Cæsarean section (Table IX) and the remainder vaginally. Four of these babies were lost. One was macerated, one was a hydrocephalic, and two had tentorial tears due to vaginal extraction through a central placenta prævia.

There was a marked rise in post-partum hæmorrhage over the age of 35 years, and a corresponding rise in the number of manual removals of the placenta.

TABLE IX.
Indication for Cæsarean Section Without Labour.

Indications.	Number of Cases.	Fœtal Results.
Over ten years' sterility and essential hypertension.	3	3 alive.
Breech presentation with radiologically contracted pelvis.	2	2 alive. 1 congenital malformation.
Fœtal distress before labour	3	3 alive.
Pelvic fibroid tumours	2	2 alive.
Flat pelvis with unengaged head ..	1	1 alive.

Perinatal Results.

The perinatal results are set out in Table XI.

Fifty-seven babies weighed less than 5 lb. 8 oz. (2500 grammes) at birth and were classified as premature. Of these babies, 19 were delivered by patients in Group IV.

There were seven intrauterine deaths before the onset of labour; one was due to an ante-partum hæmorrhage, one was due to preeclamptic toxæmia, and for the remainder no cause could be found.

There were six stillbirths; three were due to preeclamptic toxæmia, one was due to an accidental hæmorrhage following an external version, one was due to a difficult forceps delivery after a long labour, and the cause of one was unknown.

There were five neonatal deaths. Two babies weighed under 2 lb. (1000 grammes). One was post-mature and two were extracted by the breech, as was mentioned earlier.

The total loss was 18 (4·4%).

Among the 261 patients booked before the sixteenth week of pregnancy there was a fœtal loss of 7 (2·7%).

Discussion.

There is no doubt that a primipara, as she becomes older, is of necessity subjected to an increasing amount of obstetrical interference, and once she acquires the title "elderly" this rises rapidly.

There appears to be considerable variation in the age at which this title "elderly" is acquired. De Lee and Greenhill (1951) state that after the age of 35 years there is an increased incidence of toxæmia, abnormal presentations and placenta prævia. Fredrikson and Anberg (1956) add to this longer labour and increased interference in the form of forceps delivery and Cæsarean section, and Points (1957) includes increased incidence of prematurity and greater perinatal mortality.

While in this series it is recognized that the number of cases is not large, preeclamptic toxæmia and breech presentations occurred equally in each age group.

All cases of placenta prævia occurred in women aged over 35 years, and two of the three cases in women aged over 37 years.

Labour was longer in the over 37 years age group; but the average duration in all groups is some two or three hours shorter than that quoted by Fredrikson and Anberg (1956). Prolongation of labour occurred much more frequently in Groups III and IV (28 cases) compared with Groups I and II (14 cases).

All but one of the cases of Cæsarean section without labour occurred in patients aged over 37 years.

There was a sharp increase in the forceps delivery rate over the age of 35 years, rising to 51% in Group IV.

Of the premature babies delivered, 33% came from Group IV.

The perinatal mortality rate among patients seen before the sixteenth week was 0·8% in Groups I and II, and 5·3% in Groups III and IV.

With the exception of those referring to preeclamptic toxæmia, these figures agree with other published figures over the last 10 years. However, it is suggested that for this particular series the primipara becomes elderly at the age of 37 years.

Table XII sets out the complications she is liable to incur. In spite of these figures, the elderly primipara has a 72% chance of a normal, spontaneous labour, and a 92% chance of obtaining a live, healthy child.

Conclusions.

1. Primiparæ aged over 35 years do not have the same success as women 10 years younger, as shown by the perinatal mortality rate of 8% in the former groups and 1% in the latter group.

TABLE X.
Method of Delivery and Complications.

Group.	Normal Vertex Delivery.	Twin Pregnancy.	Breech Delivery.		Forceps Delivery.	Cæsarean Section.	Post-Partum Hæmorrhage.	Manual Removal of Placenta.
			Vaginal.	Cæsarean.				
I	84	1	2	—	15	0	2	1
II	72	4	5	—	27	0	2	2
III	45	2	5	—	47	5	7	10
IV	32	0	2	2	51	15	7	9

2. The perinatal mortality rate among women aged over 35 years who came under care before the sixteenth week of pregnancy was 6%, but among those whose ante-natal care commenced later it was 12%.

3. In this series women aged over 37 years are subjected to the maximum of obstetrical interference, and it is at this age level that the title "elderly" is bestowed.

TABLE XI.
Perinatal Results.

Outcome for Fœtus.	Group.			
	I.	II.	III.	IV.
Fœtal distress during labour ..	7	16	17	24
Resuscitation required	8	13	8	6
Premature by weight (5·5 lb. or 2500 grammes and under) ..	11	13	14	19
Intrauterine deaths	0	1	1	5
Stillbirths	0	0	5	1
Neonatal deaths	1	0	2	2
Congenital abnormalities	2	1	5	3
Live babies	100	103	94	92

4. The high rate of application of forceps (51%) and the high Cæsarean section rate (15%) in the elderly primiparæ were accomplished with a low fœtal mortality, as is shown in the tables.

5. In this series the best age group to have the first child is 25 to 28 years, for the following reasons: (*a*) there is the greatest number of live babies; (*b*) there is the highest incidence of twins; (*c*) the incidence of pre-eclamptic toxæmia is lowest; (*d*) the incidence of ante-partum hæmorrhage is lowest.

TABLE XII.
Complications Affecting Elderly Primiparæ.

Complication.	Percentage Occurrence.
Preeclamptic toxæmia ..	8
Ante-partum hæmorrhage ..	Placenta prævia, 2 Accidental hæmorrhage 2
Prematurity	33
No labour (elective Cæsarean section).	10
Induction of labour ..	18
Prolonged labour	12
Forceps delivery	51
Cæsarean section, excluding no labour.	5
Post-partum hæmorrhage	7
Manual removal of placenta	9

Summary.

1. Four hundred first pregnancies and labours are examined in four age groups, from very young to elderly.

2. The complications, perinatal mortality and fœtal survival are assessed and compared.

3. It is suggested that the elderly primipara in this series is aged 37 years and over.

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References.

BROWN, F. J., and BROWN, J. C. McC. (1955), "Ante-Natal and Post-Natal Care", 8th Edition, Churchill, London: 338.

DE LEE, J. B., and GREENHILL, J. P. (1951), "Principles and Practice of Obstetrics", 10th Edition, Saunders, Philadelphia and London: 603, 632.

DENNEN, E. H., and AINSLIE, W. H. (1951), "The Elderly Primipara", *Postgrad. med. J.*, 10: 241.

FREDRIKSON, H., and ANBERG, A. (1956), "Delivery of Elderly Primigravidas", *Acta. obstet. gynec. scand.*, 35: 483.

HARVEY SUTTON, D. (1945), "Gestation Period", MED. J. AUST., 1: 611.

OSTRY, E. I. (1955), "The Effect of Delay in the First Stage of Labour on the Forceps Rate and on the Stillbirth and Neo-natal Mortality Rates", *J. Obstet. Gynæc. Brit. Emp.*, 62: 115.

POINTS, T. C. (1957), "The Elderly Primipara", *Obstet. and Gynec.*, 9: 348.

STEVENSON, R. B. C. (1958), "The Prevention of Eclampsia and Severe Pre-eclampsia", *J. Obstet. Gynæc. Brit. Emp.*, 65: 982.

STURROCK, J., and BROWN, R. (1956), "Prolonged First Stage of Labour", *J. Obstet. Gynæc. Brit. Emp.*, 63: 83.

TOWNSEND, L. (1959), "High Blood Pressure and Pregnancy", Melbourne University Press: 2.

SOME ASPECTS OF REHABILITATION OF THE CARDIAC DISABLED.[1]

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THE purpose of this report is to bring to the notice of the medical profession our experience with a group of cardiac patients handled by the Rehabilitation Medical Section of the Department of Social Services, Brisbane, over a five-year period ending in June, 1959. The patients were selected by a panel of doctors from a group of social service beneficiaries who had been receiving a benefit for more than three months—invalid pension, sickness benefit, unemployment benefit. In addition, there was a small miscellaneous group comprising adolescents and patients referred by the Workers' Compensation Office. The aim of selection and therapy was ultimate placement in full-time remunerative employment.

There were 130 cases in all in the retrospective survey. I was associated with 58 cases, 72 being handled by other members of the present panel. Diagnosis was correct in 111 cases, incorrect in 19 cases, or some 15%. This is higher than the over-all figure for misdiagnosis in such cases, owing to selection. In the group were country cases not fully investigated previously. The final diagnosis was not arrived at in some cases until after a period of observation and assessment of cardiac function and personality by a team including psychiatrists and therapists at the Day Attendance Centre. Common errors were benign murmurs diagnosed as rheumatic fever, and hysteria masquerading as ischæmic heart disease, coronary sclerosis and paroxysmal tachycardia. Terms used in certification such as weak heart, leaking valve, heart complaint, heart disease, heart weakness, cardiac and myocardial insufficiency, and strained heart, are as objectionable on the grounds of scientific accuracy as they are damaging to the patient's morale.

[1] Part of a panel discussion presented at a joint meeting of the Queensland Branch of the British Medical Association and senior members of the section of Rehabilitation and Physical Medicine, Brisbane, September 17, 1959.

Analysis of Material.

Seventy-four subjects were recipients of an invalid pension, 33 of sickness benefit and 15 of unemployment benefit. There were three adolescents, and five patients were referred by the Workers' Compensation Office.

Forty-four patients had rheumatic heart disease, 40 had ischæmic heart disease, and there were 23 cases of congenital heart disease. Fourteen patients were suffering from cardiac neurosis, but had normal hearts, six had hypertension, and there was a small miscellaneous group of four cases. The bias of selection favoured rheumatic and congenital heart disease, owing to the large number of invalid pensioners in the group.

Forty-six subjects were in the 15 to 25 years age group, 14 in the 25 to 35 years group, 28 in the 35 to 45 years group and 42 in the 45 to 55 years group. The early age group was so large because of the incidence of rheumatic and congenital heart disease; ischæmic heart disease swelled the ranks in the 35 to 45 years group.

Thirty-six patients were classified as unskilled labourers; 26 were semi-skilled and skilled workers, requiring moderate physical exertion in the course of their work; 31 were sedentary or light workers; 31 had no occupation; three were unclassified.

Most of the patients had moderate disability or less. As the goal was full-time employment, patients with severe disability were discounted; there were, however, 21 patients with moderately severe disability.

Cardiomegaly was found to be the most reliable objective indication of a patient's disability and ultimate prognosis. Assessment was primarily by physical examination, but in most accepted cases this was confirmed and amplified by electrocardiography and radiography. For convenience, the heart size was graded as normal, or enlarged (Grades I to IV in increasing severity), largely on the basis of clinical experience. Fifty-eight patients had normal-sized hearts, 32 had Grade I enlargement, 15 had Grade II enlargement, 15 had Grade III enlargement and one had Grade IV enlargement. Grading was not made in seven cases.

There was a wide spectrum of complicating physical diseases, some of which were more effective than the cardiac lesion in rendering the patient unemployable.

The high incidence of personality defects in this selected group is both impressive and disturbing. Moreover, it is undeniable that much of this morbidity is definitely preventible. Medical teaching has long paid lip service to the dictum that organic disease occurs as but an incident in the patient's life, and that treatment of the whole man is a desideratum of rational therapy. It is obvious that practice all too often falls far short of preaching. Hysteria and chronic anxiety were the most common personality aberrations. There were 15 instances of cardiac neurosis, 12 of immaturity and eight of inadequate personality. Nine patients had low intelligence and 10 were educationally retarded. Only one patient had a frank psychosis, and four patients had a pension fixation. Eight were negativistic to all efforts to help them. Of 98 patients for whom an assessment was made, only 25 of 66 males and 5 of 32 females were thought to have normal personalities. The medical profession must be held largely responsible for the high incidence of immaturity and educational retardation among young people with rheumatic or congenital heart disease.

Sixty-three patients out of 107 were regarded as being suitable for rehabilitation, of whom 36 were invalid pensioners and 18 recipients of sickness benefit. Forty patients were rejected, eight are still being investigated, and 15 ceased to receive a benefit during the course of investigation, more or less directly as a result of departmental action. The main reasons for summary rejection for rehabilitation were severity of disability, personality defect and age.

Analysis of Accepted Cases and Results.

There were 15 subjects with ischæmic heart disease, all male; 10 were successfully reemployed and one is still being rehabilitated. There were four failures; one of these patients worked for one year. Personality defect was the chief cause of failure (three cases out of four). Favourable factors in prognosis are sound personality, normal or near-normal effort tolerance, slight change in the electrocardiograph, lack of cardiomegaly, positive management, reassurance and explanation, educability and possibility of selective job placement. The time taken for rehabilitation in successful cases ranged from two weeks to ten months; the average was 2·5 months.

The 25 accepted subjects with rheumatic heart disease had varying lesions; six had aortic regurgitation (four severe) and seven had mixed aortic and mitral disease. Of two patients with aortic stenosis, one was referred for aortic valvotomy. Nineteen patients were successfully rehabilitated and two are still being treated; there were four failures (one of these patients worked for one year). The time taken for rehabilitation in successful cases ranged from 4 to 44 weeks; the average was 16 weeks. Again, personality defect was found to be twice as common as the severity of the lesion in causing failure among accepted cases. Favourable prognostic features were similar to those noted in dealing with patients with ischæmic heart disease. The large number in the 15 to 30 years age group was a help. Only those with high intelligence among patients with moderately severe disability may be rehabilitated.

Sixteen cases of congenital heart disease were dealt with; in three of these the abnormality was tetralogy of Fallot, and the remainder were spread over the common acyanotic varieties of congenital heart disease. All three patients with the tetralogy of Fallot were operated on, as were the three with patent ductus and the two with coarctation of the aorta. Nine cases were successfully dealt with, there were two failures, and five cases are current. Of the failures, one patient had, in addition to a patent ductus, deafness, mental defect, recurrent bronchitis and poor physique—an instance of faulty case selection; the other failed in suitable work as a result of personality defect. The average time taken for rehabilitation in successful cases was 8·5 weeks, with a range of 4 to 12 weeks. This figure is artificially low, as several long-term cases are still in the current group.

There was a miscellaneous group of seven cases, mainly instances of faulty diagnosis tinctured with an underlying hysteria. Of these patients, five were successfully placed in work; the two failures were due to personality defect.

It is strange that there were no hypertensives among the accepted subjects. These patients tend to select themselves out of this survey, as they remain in work until they are too severely disabled to come within the scope of this service.

Thus it may be seen that the over-all results were 43 successes, 12 failures and 8 cases not yet concluded. This assessment is made from a strictly vocational and placement aspect. In point of fact, very few (about five) of the accepted patients failed to show symptomatic and psychological improvement after therapy. It would seem that evaluation and case selection are adequate. The results are surprisingly good, considering the nature of the material.

It is an opportune time to consider the economic implications of this work. The life expectation of this group is indicated by the fact that only four patients out of 130 died in the five years of the survey. Working on the basis of a working life of 12 years for rheumatic and congenital heart patients and eight years for ischæmic heart patients, and arbitrarily selecting five years for the miscellaneous group, if £200 a year is allowed for benefits, the saving on the 43 successful cases amounts to some £88,000. The cardiac disabled are only a small proportion of patients being treated in the rehabilitation centre, something less than 5%.

Discussion.

The problem of rehabilitation of the cardiac disabled is becoming increasingly great. Ischæmic heart disease is on the increase. The use of anticoagulants is increasing the longevity but not affecting the morbidity of patients with ischæmic heart disease. Palliative surgery is improving life expectancy in rheumatic and congenital heart disease, and the use of antibiotics is lowering the risk of lethal complications in all groups. There is an increasing group of partially disabled in the community, which is at present unproductive and a drain on the public purse. Politically, it cannot be ignored. Until preventive medicine can render rehabilitation obsolete—probably not in our time—our attack must be two-pronged: (i) reduction of the numbers and morbidity of the disabled to a minimum; (ii) provision of facilities whereby the residual capabilities of the disabled may be profitably used.

Most workers find that over 85% of the aged, unskilled cardiac disabled cannot be rehabilitated. Genuine disability must remain the greatest single factor militating against reemployment under our persent conditions. Heart size and effort tolerance are of little more significance than personality factors in assessing the possibility of reemployment of patients who have been for prolonged periods receiving a social benefit. A hard core of incorrigible personality defects will always remain as the third greatest factor militating against reemployment. Cardiac neurosis, the second largest factor, is largely preventible. This entails better education of the patient, the doctor and the employer. Handling of cardiac patients—and this includes the relatives of minors—must be more positive. Loose speaking is as damaging as loose thinking.

The doctor should be better educated at undergraduate and post-graduate level in the philosophy of his art no less than in the science. Diagnosis should be as accurate as possible, and the natural history of the various forms of rheumatic and congenital heart disease should be more widely appreciated. Patients in these groups should be encouraged to equip themselves for as full a life as possible. They should be better educated than average to fit them for light occupations; educational retardation, often the result of needless medical proscription, is far too common in this group. Intelligent handling by the doctor should minimize the tendency to immaturity and parental over-protection, which all too often renders these patients unacceptable to employers who have work to offer that is well within their physical capability. Reassurance and explanation of the true prognosis of ischæmic heart disease should, in another generation, dissipate the spectre that angina pectoris has been in the past and is considered still by many doctors and their patients. Employers must be made aware of the following facts in relation to cardiac patients who are properly placed: absenteeism and turnover are not major problems; few experience cardio-vascular episodes while at work; they are safe workers, and their average productivity is no less than that of non-cardiac employees. It must be realized by industrial management and executive that an increasing unproductive pension group, through growing social service contribution for benefits, medical attention and drugs, is pricing our goods out of competitive world markets. Two approaches spring to mind: (i) the reservation of a certain number of light jobs in industry for the partially disabled; (ii) the creation of sheltered workshops where the disabled can do part-time or full-time work within their capabilities. Unless more avenues of suitable placement can be found, it must be seen that further attempts at rehabilitation of the cardiac disabled will prove fruitless.

It must be obvious to all observers that this essay into rehabilitation barely touches on the fringe of an increasingly important medico-social problem.

Summary.

1. A five-year retrospective survey has been made of 130 cases of cardiac disability handled by the Rehabilitation Medical Section of the Department of Social Services, Brisbane.

2. Of 63 accepted cases, 55 have been terminated, with 43 patients successfully returned to full-time remunerative employment.

3. The importance of personality factors in this disease group has been emphasized.

4. The medico-social importance of cardiac disability is stressed, and suggestions are put forward for interim measures to combat the morbidity resulting from it.

Acknowledgements.

My gratitude is due to Dr. Gordon MacLean, who initiated this work and encouraged this review; to my fellow workers, medical and lay, of the Rehabilitation Medical Service at Kingshome, without whose cooperation and enthusiasm this work would never have come to fruition; and finally to Mr. A. W. Cox, Director of Social Services, Brisbane, for permission to consult departmental records.

THE MANAGEMENT OF VARICOSE ULCERS.

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IN medical practice today there must be few conditions as common as varicose ulcer still presenting a challenge for their correct appraisal and treatment. Though the basic facts of its causation have been known for over 100 years, it is only in comparatively recent times that attention has been refocused on the essential problem—faulty venous hæmodynamics. Despite the spate of articles on this subject in the last ten years, there still seems to be widespread failure to appreciate the problems or to institute rational treatment.

"Varicose ulceration" is common. Estimates of its incidence vary, but they understate the frequency. Many patients, disheartened by actual or reputed lack of successful treatment, do not report. It is unfortunately true that few doctors can evince any interest in the plight of these patients, often suffering severe pain, with socially unattractive and smelly legs covered with bandages.

Apart from its morbidity, varicose ulceration is a frequent cause of change of employment, often to a less well paid "sitting down" job. The economic loss to the country as a whole must be tremendous. Curwen and Scott (1952) estimated that in the United States nearly six million working days were lost annually from varicose ulceration and the effects of varicose veins.

Pathology.

The exact pathogenesis of varicose ulceration is not entirely understood, but the basic facts are clear. Though varicose ulcers are often associated with superficial varicosity, this is not essential, and often it is not relevant to their formation. Severe superficial varicosity may exist, even for prolonged periods, without ulceration, and may be merely a pointer to the underlying disease of the deep and/or communicating veins. The term "varicose ulceration" is justified only by its established usage and not because of its ætiological associations.

H. E. Lockhart-Mummery and Smitham (1951) segregated the patients with simple superficial varicose veins and no complications from (i) those with pigmentation, induration and ulceration of the lower third of the leg, but no varicose veins, and (ii) those with varicose veins in the thigh or leg, and ulceration.

It is these—the ulcer groups—which have in common locally raised venous and therefore capillary pressure with resultant œdema. The œdema is quite different from that of cardiac or renal origin, and is probably due to capillary damage allowing escape of proteins, fibrin formation and consequent organization and fibrosis, leading to inter-

ference with local blood supply and further capillary damage—a vicious circle initiated by œdema from raised venous pressure.

The raised venous pressure is due to the following two abnormalities: (i) incompetent deep veins—either primary "essential" varicosity or incompetence resulting from irreparable damage to valves by thrombosis (these changes may be general or local in extent); (ii) failure of the calf muscle pump to propel the blood supply against gravity, when there are no functioning valves to prevent reflux. In the presence of reflux, venous pressure in the leg rises instead of falling when the leg is used.

The actual ulcer is most often precipitated by trauma, commonly of a minor degree; secondary infection supervenes. What determines the extension and final extent of ulceration is not known. The almost constant situation of these ulcers is probably determined by the anatomical sites of the incompetent communicating veins, as shown by the work of Cockett and Jones (1953).

Though the essential prerequisite for ulceration is œdema consequent upon venous reflux and raised venous pressure, other factors in tissue metabolism may play a part in retarding healing and repair—for example, nutritional deficiencies (vitamins, iron, proteins, etc.), insufficient local arterial and capillary blood supply, generalized disease (especially cardiac and renal disorders and diabetes) and infection (bacterial, or rarely fungal).

Diagnosis.

The diagnosis, though often obvious from the history, demands more than the usual cursory inspection that is made. Successful treatment can result only from a full assessment of all factors. This demands (i) a complete history and examination of the stripped patient in a good light, and in certain cases laboratory investigation, and (ii) time to explain the principles of treatment to the patient, and to the person who carries out the treatment.

The constant site of the ulceration in a swollen leg discoloured by "varicose" eczema and pigmentation, often looking like an "inverted bottle", is so diagnostic that other causes of ulceration which can closely resemble "varicose ulcer" are often overlooked and forgotten. It is, however, important to exclude the following: (*a*) ulcers due to the arterial insufficiency alone; (*b*) traumatic ulcers, which may be slow to heal; (*c*) ulcers in atrophic skin—for example, the site of an old burn; (*d*) ulcers overlying an area of chronic osteomyelitis; (*e*) primary squamous cell carcinoma, or neoplastic change in a chronic ulcer; (*f*) ulcers from rare causes—syphilis, tuberculosis, ulceration in an area of dermatitis artefacta.

The general examination of the patient must assess the following: (i) the general health, and especially nutritional deficiencies and/or obesity; (ii) general diseases coexisting with, or contributing to, the leg condition—for example, diabetes, or cardiac, hepatic or renal diseases contributing to deficient oxygenation, deficient arterial transport, raised venous pressure or œdema; (iii) obstruction in pelvis, abdomen or chest to venous return from the legs; (iv) the state of arterial and capillary circulation in the leg; (v) pathological conditions of the veins of the leg, both superficial and deep, and including the "calf muscle pump"; (vi) (*a*) the state of the ulcer (site, size, shape, edge, base, fixity, surrounding tissues), (*b*) œdema of the leg; (vii) the condition of the other leg.

Treatment.

The aims of treatment are as follows: (i) to diagnose the ulcer correctly—its ætiology, its pathogenesis and all contributing factors; (ii) to heal the ulcer; (iii) to keep it healed.

The essential "pathology" is œdema. It is this which causes the ulcer and keeps it in existence. Almost all ulcers will heal when œdema is controlled. Infection, inevitable in an ulcerated surface, has received undue attention, and its control is not of primary importance (except that of the rare fungal infection). Local or generalized varicosities have often suffered from the enthusiastic procedures of surgeons without the ulcer being cured. It is lack of understanding of ætiology that accounts for failure to heal the ulcer and keep it healed.

To Heal the Ulcer.

The sheet anchor of treatment is to abolish and control œdema by compression bandaging. Dickson Wright (1931) restated this fact, and it has been preached often since; but the lesson has not been widely learnt yet. At the annual meeting of the British Medical Association in Liverpool in 1950, it was stated to be "unfortunately still too true that simple occlusive bandaging methods are neither sufficiently well known nor properly practised" (McAusland, 1950). There is little evidence that the situation is greatly different today.

To be effective continuously, the compression bandage should easily adapt itself to the varying shape and condition of the leg, so that as œdema recedes the bandage will still effectively compress the leg. The bandage therefore needs to be elastic, but in one direction only—a one-way-stretch bandage—applied from metatarsal heads to below the knee in a continuous overlapping spiral and including the heel.

The bandage is applied in the morning before the patient rises. It is best applied by someone other than the patient (it is this person who has to be instructed in the correct method of application), though many patients find no undue difficulty in applying it themselves. A little zinc cream and gauze are applied over the ulcer itself. The bandage remains firmly on, giving elastic support throughout the day, and is removed only at night, when the patient goes to bathe or shower and then to bed. During the night the ulcer is simply covered with a piece of gauze held in place by a few turns of crêpe bandage. The one-way-stretch bandage is not worn.

The advantages of this method over all others are as follows: (i) It is constantly effective in controlling œdema whilst it is applied. (ii) It allows the patient to continue his normal habits, and is of great aid hygienically—especially in a hot climate or where work is "dirty". Patients appreciate its removability particularly at night. (iii) It allows patients to conduct their own treatment effectively while continuing their normal occupation. (iv) It is cheap. Approximately three or four yards are required per leg, and the cost is 3s. 6d. per yard. (v) The bandage is easily washed; it dries overnight, and so the usual dirty and unpleasant bandages are totally avoided.

An alternative method of applying elastic compression is by the application of an adherent "Elastoplast" bandage in the form of a stocking. Though this is effective in compression, it suffers from many disadvantages, the chief of which are the following: (*a*) Dermatitis and irritation occur in a high percentage of cases. (*b*) It is most difficult to apply correctly and often "cuts in", producing further ulcers especially over the front of the ankle. (*c*) It cannot be applied by patients, nor is it removable. (*d*) To be effective it must be applied when œdema is least—before rising; this is practically impossible in most cases, and if it is applied on a swollen leg, it loses much of its efficacy. (*e*) It interferes with the patient's hygiene and is greatly resented, especially in the summer. Its continued use is therefore not indicated, since it has been superseded by something infinitely better.

Other methods of supportive bandaging fall short of the ideals of elastic adaptability and constancy of pressure. This criticism, as well as that of non-removability, applies to the many varieties of zinc and gelatine bandages, while crêpe bandages are quite ineffective in reducing œdema if they still have any "give" and are like cotton bandages if they have no "give". Their continued use is to be deprecated.

Local application to the ulcer is not of primary importance to successful treatment. The ulcer is secondarily infected, and control of infection does not lead to healing of the ulcer. It is control of œdema that establishes con-

ditions necessary for healing. A little zinc cream is all that is required; antiseptic or antibiotic applications are not indicated, and by their properties of sensitization may even be harmful. The exception is *Mycobacterium ulcerans* infection; but this is so rare that it can be ignored for practical purposes.

Whereas elastic bandaging by its control of œdema is the major factor in promoting healing, other contributing factors must also be considered. The first of these is reestablishment of the calf-muscle pump by walking. It is unfortunately still true that many patients are vaguely instructed to "rest the leg"—the worst thing that the patient can do; it produces atrophy of the calf muscle, raises the venous pressure, and thus increases œdema (if the leg is at all below the level of the heart) as well as producing stiffening of all leg joints. Patients must be actively encouraged to walk as much as possible (three miles per day), and also instructed not to stand for prolonged periods.

Some ulcers are indolent because of lack of arterial blood supply to the part. Vasodilator drugs have, on the whole, been disappointing in their effectiveness, and in these cases lumbar sympathectomy may be indicated to induce healing. Sympathectomy is well tolerated by even frail patients. It does not work in every case; but there are no conclusive tests which will before operation indicate the likelihood of success. The test for the effectiveness of sympathectomy is to perform it.

General nutritional improvements and control of obesity are amongst the most worthwhile measures that we can institute. They are safe, sure and easy and may turn the scales towards success.

The scheme as outlined will effectively heal the majority of ulcers quickly, surely and with least trouble to doctor and patient. There remain a small percentage of patients requiring different measures—skin grafting to circumferential ulcers, and excision and grafting of those ulcers whose base consists almost entirely of fibrous tissue over which no epithelium could regrow. Cockett and Jones (1953) have made out a case for excision of the ulcer, together with the incompetent underlying communicating veins in those ulcers produced by the "ankle blow-out" syndrome, and in this group of ulcers the procedure gives excellent results.

To Keep the Ulcer Healed.

To keep the ulcer healed is most important. The principles of the factors which induced healing must be continuously observed, and again the main one is control of œdema. The basic fault lies in the incompetence of the deep veins (from whatever cause). These are as yet not amenable to surgical measures; but incompetent communicating veins, if causing the ulcer, can be dealt with surgically. Incompetent long and/or short saphenous veins may be removed by stripping if it is thought that they contributed towards the ulcer. However, it should not be done before six weeks after complete healing, during which time the leg should be adequately supported by a one-way-stretch stocking. Even after stripping the leg may need further support. The great majority of patients, however, require continued or lifelong support. This can be provided by means of the one-way-stretch bandage or more easily by means of a one-way-stretch elastic stocking. To be effective, an individual seamless stocking including a heel must be made for the patient. Unfortunately manufacturers and surgical supply shops can only with difficulty be persuaded to manufacture individual stockings, preferring to stick to their standard sizes and models with absent heels (so that local œdema occurs there). When ordering stockings it is important to measure the patient's leg (i) at the instep, (ii) round the ankle, (iii) round the calf, (iv) just below the knee, (v) from the knee to the heel and (vi) from the heel to the metatarsus, and to insist on individual stockings being made. Two-way-stretch or the asthetically satisfactory type of stockings produced commercially for this purpose are quite useless and do not control œdema effectively. A properly fitting one-way-stretch stocking tends to wear out in three to four months, and must be replaced frequently if the control of œdema is to remain effective. The stocking is applied by the patient in the morning before rising. Patients must be instructed in order to keep their ulcer healed, (i) not to walk about without their stockings (except when retiring); (ii) to avoid all trauma to their leg; (iii) to keep their leg clean; (iv) to report immediately if another ulcer forms or eczema reappears; (v) to continue the general health measures instituted, especially walking and keeping the weight down; (vi) to replace the stocking frequently—before it is worn out.

Conclusion.

A patient relieved of his ulcer, with a leg that is once more a useful member, is a patient grateful and useful, and a sure sign that this Cinderella of medicine requires only understanding of its cause and application of this knowledge.

References.

COCKETT, F. B., and ELGAN JONES, D. E. (1953), "The Ankle Blow-Out Syndrome. A New Approach to the Varicose Ulcer Problem", *Lancet*, 1: 17.

CURWEN, I. H. M., and SCOTT, B. O. (1952), "The Ambulant Treatment of Complications Resulting from Varicose Veins and Allied Conditions", *Ann. phys. Med.*, 1: 17.

DICKSON WRIGHT, A. (1931), "The Treatment of Indolent Ulcers of the Leg", *Lancet*, 1: 457.

MCAUSLAND, S. (1950), "The Importance of Bandaging", Section of Surgery, 118th Annual Meeting of the British Medical Association, Liverpool, *Brit. med. J.*, 2: 270.

LOCKHART-MUMMERY, H. E., and SMITHAM, J. H. (1951), "Varicose Ulcers. A Study of the Deep Veins with Special Reference to Retrograde Venography", *Brit. J. Surg.*, 38: 284.

A FURTHER EXAMPLE OF ANTI-By (BATTY) IN THE SERUM OF A WOMAN WHOSE RED CELLS ARE OF THE $A_x(A_0)$ SUBGROUP OF GROUP A.

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SIMMONS AND WERE (1955) found that a direct positive Coombs reaction obtained on the erythrocytes of a newborn child was due to coating with a hitherto undescribed antibody, anti-By. It was present in an incomplete form in the maternal serum, and the corresponding antigen was demonstrated in the erythrocytes in four out of eight members of the By (Batty) family. It was absent from 500 random blood samples tested at the time by the indirect Coombs test. The authors considered the By system as a "family" one. However, since the publication of their paper, one other example of this antibody and two examples of the antigen have recently been discovered in England, and the position of By has therefore moved from the "family" systems to that of the rare "public" ones (Cleghorn, 1959). A routine search conducted in Melbourne and in Brisbane for further examples of anti-By revealed one in about 1400 serum samples tested. This atypical antibody was found in the serum of a pregnant woman (Mrs. M.), who, although no problem for the obstetricians (as she was delivered of a healthy normal child), was of considerable interest to the serologists. Not only did her serum contain this rare antibody, anti-By, but her erythrocytes behaved irregularly, as they belonged to an uncommon subgroup of group A.

The purpose of this paper is to discuss the antibody anti-By and the unusual group A antigen encountered in the same individual.

MATERIALS AND METHODS.

By the use of known By-positive erythrocytes, serum from normal blood donors and from pregnant females (before or after delivery) was tested for the presence of anti-By by the indirect Coombs test, or with the aid of a papain solution. Experience has shown that the original incomplete anti-By, which had an indirect Coombs titre of about 1:40, reacted well with papain-treated erythrocytes.

The Anti-By Antibody in Mrs. M.'s Serum.

At the time of the discovery of the present By antibody, Mrs. M. was pregnant for the second time. Her first pregnancy had terminated one year previously with the birth of a still-born child. There was no history of blood or other transfusions. In addition to group-specific agglutinins, her serum contained an incomplete antibody demonstrable by the indirect Coombs method, and in the presence of papain; this antibody reacted initially with two samples of By-positive cells, one obtained from Mr. By, and the second from another By-positive individual, kindly sent to us by Dr. T. E. Cleghorn of Sutton, England. The serum also reacted with cells from the three Batty children known to possess the By antigen. It did not react with cells containing antigens of other known blood-group systems and was therefore classified as anti-By. Its titre was 1:64 in serum samples collected two months prior to delivery, at delivery and eight days later. The baby's cord cells, which were of Group O, gave a negative response to the Coombs test, and did not react with the maternal serum either by the indirect Coombs test, or after treatment with papain, or by the indirect Coombs test with these papain-treated cells. The anti-By antibody was present in the cord serum at a titre identical with that in the maternal serum.

Mrs. M.'s A-B-O Pattern.

Erythrocytes.

When tested against standard commercial A-B-O blood-grouping sera issued by the Commonwealth Serum Laboratories, Mrs. M's erythrocytes gave the reactions as shown in Table I.

TABLE I.

Initial Reactions of Mrs. M.'s Red Cells in A-B-O Grouping.

Antiserum.	Response.
Anti-B from Group A donors	Negative.
Anti-A from Group B donors[1]	Negative.
Anti-A_1, human origin	Negative.
Anti-A_1, *Dolichos biflorus* extract ..	Negative.
Anti-A plus Anti-B from Group O donors	Positive.

[1] See results of subsequent tests with 16 batches of commercial anti-A sera, in which 8 gave no agglutination and 8 reacted in varying strengths.

The anti-A content of Group B and Group O antisera used in the initial tests proved to be very similar when titrated with A_1 and A_2 cells. Mrs. M.'s cells were then tested with a further 16 batches of commercial anti-A (Group B) serum with titres comparable with those used above, and of these, eight did not agglutinate Mrs. M.'s cells, six gave very weak agglutination, one gave moderate agglutination, and with only one serum did the test cells give a reaction approaching that given by A_2 cells.

Mrs. M.'s cells reacted with all 13 anti-A plus anti-B (Group O) commercial sera with which they were tested, although agglutination was weaker than with A_2 cells.

After contact of Mrs. M.'s erythrocytes with an anti-A serum, anti-A could be eluted from them, although they were not agglutinated by this anti-A serum, and did not reduce its titre for A_1 cells. The amount eluted was small, and was less than that obtained by absorption and elution from A_2 cells. Eluates from Mrs. M.'s cells after contact with Group O serum showed a higher reactivity with A_1 cells than did eluates from A_1 or A_2 cells after contact with the same Group O serum.

Serum.

Apart from the incomplete anti-By and group-specific anti-B agglutinin (titre 64), Mrs. M.'s serum agglutinated A_1 cells at 22° C. (+) and at 5° C. (+++).

Saliva.

No A substance was demonstrated in Mrs. M.'s saliva.

DISCUSSION.

The A Subgroup in the Red Cells.

Since von Dungern and Hirszfeld indicated the existence of subgroups of A in 1911, numerous further subgroups and variations of the very complex Group A antigen have been reported. Their descriptions and designations have been occasionally overlapping, leaving a bewildering accumulation of numbers and letters (A_1, A_2, A_3, A_4, A_5, A_x, A_0, A_z, A_m, A_E) all attached to the major designation "A". Recent papers on the A subgroups have been published by Cahan, Jack, Scudder, Sargent, Sanger and Race (1957), by van Loghem, Dorfmeier and van der Hart (1957), by Weiner, Lewis, Moores, Sanger and Race (1957) and by Celano, Levine and Lange (1957), and the subject has been further reviewed by Race and Sanger (1958). Eight properties were defined for the A_2, A_3, A_4, A_5, etc., subgroups by Grove-Rasmussen, Soutter and Levine (1952), which are as follows:

First, their cells give but weak reactions with potent anti-A serums derived from group B donors.

Second, they fail to react with weak or absorbed anti-A serums from group B donors.

Third, they usually will be agglutinated more markedly by O serums than by B serums.

Fourth, their absorption avidity toward the anti-A agglutinins is not as great as that of A_1 cells.

Fifth, elution experiments have shown that it is easier to separate absorbed isoagglutinins from them than from A_1 cells.

Sixth, their agglutination reactions are less pronounced when produced by high titered anti-A serum from B donors, if that titer is natural, than if it were induced by the use of Witebsky's A and B specific substances.

Seventh, the strength of their agglutination reactions with anti-A serums from B donors has a variability not entirely dependent on the titer of these serums.

Lastly, the A_2 and weak A_3 subgroups may have anti-A_1 in their serums as a naturally occurring antibody.

The above authors then described a new subgroup which they called A_0. Its significant characteristic is complete lack of agglutinability by Group B sera (15 of 15 failed to react) and good agglutinability by Group O sera (44 of 50 reacted).

While some of the A variations encountered now appear to have been caused by disease conditions (van Loghem *et alii*, 1957; Stratton, Renton and Hancock, 1958), others are permanent, and the latter fall roughly into two categories: (i) those due to the action of modifying or suppressor genes (*yy*); (ii) those due to variation in quantity or quality in the A antigen itself.

The suppressor gene *y* of the A system, when present in double dose, modifies the development of A antigen in the erythrocytes, but does not prevent its appearance in saliva. Two such cases were described by Weiner *et. alii* (1957). Subgroup A_m described by Wiener and Gordon (1956), in which the erythrocytes reacted as Group O, the serum lacked anti-A and the saliva contained A substance, may be another example of gene modification. As Mrs. M.'s erythrocytes show some of the A character and as her saliva does not contain any A substance, she apparently does not belong to the first category. Her A-B-O pattern, however, seems to have the features described for the second category, which consists of A_x (A_4, A_5, A_z, A_0) as listed by Race and Sanger (*loco citato*), and possibly the factor C as described by

Wiener (1953). The A_x subgroup is characterized as follows. The A_x cells in the presence of anti-A serum do not agglutinate or agglutinate weakly; they fail to agglutinate with anti-B serum, but agglutinate with most anti-A plus anti-B (Group O) sera. The agglutination with Group O sera while weak is general, and not like that of A_3, where many cells remain unagglutinated. A_x individuals who are secretors do not secrete the A antigen in their saliva. Further, A_x cells, although not agglutinated by anti-A, absorb anti-A, because anti-A can be demonstrated in their eluate.

In comparison, Mrs. M.'s cells were agglutinated by 8 out of 17 commercial (pooled) anti-A sera, failed to agglutinate with anti-B sera, but agglutinated with 13 out of 13 commercial anti-A plus anti-B (Group O) sera. Her saliva did not contain A substance, while her serum contained anti-B and anti-A_1. To separate members of the A_x subgroup is rather difficult, and as Race and Sanger state:

> In general it is wise to avoid giving specific names to samples that merely represent different parts of a normal distribution curve of antigen strength.

Mrs. M.'s erythrocytes and saliva react very much like those of the "A_x" persons first described by Fischer and Hahn (1935). But Mrs. M.'s serum did not possess an exceptionally high anti-B titre, nor did it have an unusually high concentration of hetero-agglutinins or hetero-hæmolysins against sheep cells, as Fischer and Hahn described in their A_x persons. If A_x is accepted as a descriptive symbol for A cells which are preferentially agglutinated by anti-A of Group O sera, and there are further subdivisions within this subgroup, then Mrs. M.'s cells bear some similarity to subgroup A_o reported by Grove-Rasmussen *et alii* (*loco citato*). Absorption and elution results are almost identical, as are the absence of A substance in saliva and the presence of anti-A_1 in the serum, although the latter was apparently more marked in our case than it was in the former. However, it should be noted that in tests with the original A_o blood sample, none of 15 Group B sera agglutinated the cells, while Mrs. M.'s cells were clumped to some degree by 8 out of 17 commercial Group B sera with which they were tested, behaving in this respect similarly to a second example reported as A_o by Engelfried (1955).

Wiener's blood factor C also gives the reactions described for Mrs. M.'s blood, although it is theoretically based on a different conception of these reactions. According to Wiener, the agglutinogens A and B contain the factors A and C and B and C respectively. Anti-C is present in sera derived from Group O persons, but lacking in sera derived from Group A and Group B persons. The amount of C in human erythrocytes varies. According to this concept of a mosaic structure of the antigen, Mrs. M.'s cells contain mainly C and very little A, thus reacting with the anti-C of Group O sera, but only negligibly with pure anti-A. The cells might therefore be classified as C_A (Wiener and Wexler, 1958).

The value of using all three testing sera, anti-A, anti-B, and anti-A plus anti-B, for routine and medico-legal A-B-O blood grouping is again demonstrated, and this has been the regular practice in our own and most Australian laboratories for over 25 years. The use of the three testing reagents is strongly recommended for accurate A-B-O blood grouping.

The By Antibody in the Serum.

The By antibody in Mrs. M.'s serum was of the incomplete type with a titre of 1:64. Although it was placenta-permeable, being present in the cord serum, it could cause no damage to the child, as the cord cells lacked the corresponding By receptors. Unfortunately the husband's cells could not be obtained for testing for their By group, and we are therefore not able to state definitely that the production of this By antibody was unconnected with the previous (first) pregnancy. However, it should be remembered that maternal sensitization by the first fœtus is very rare, and the second did not possess the antigen to produce a titre of 1:64. As Mrs. M. has never received a blood transfusion, it appears probable that the By antibody was not caused by immunization with By antigen derived from human red cells. The By antibody is not common, as it was revealed only once in about 1400 tests made in a deliberate search of maternal and blood donor sera.

Summary.

An example of the By (Batty) blood-group antibody is described. It was found in the serum of a woman, Mrs. M., both before and after delivery of a By-negative child. The possible origin of this antibody is discussed.

The subgroup A_x (A_o) erythrocytes of Mrs. M. were agglutinated by 13 out of 13 commercial (pooled) Group O sera. They were not agglutinated by 9 out of 17 commercial (pooled) Group B sera, were weakly agglutinated by 6, and gave moderate agglutination with one, and with only one did the strength of reaction almost approach that given by A_2 cells.

An eluate from Mrs. M.'s cells after contact with non-agglutinating Group B sera acted weakly on A_1 cells.

An eluate from Mrs. M.'s cells after contact with Group O sera had a higher anti-A titre than eluates from A_1 or A_2 cells.

The anti-B titre of Mrs. M.'s serum was 64. The serum also contained a cold agglutinin of anti-A_1 specificity. No A substance was demonstrated in the saliva. As Mrs. M.'s second child was shown to be of Group O, her own A-B-O genotype could be A_xO.

The position of Mrs. M.'s cells within the broad A_x, A_o and C subgroups is discussed.

Addendum.

Since submitting this paper for publication, Mr. M's blood has been shown to be of subgroup A_1, and his red cells lack the By (Batty) antigen. In the absence of obvious antigenic stimulus the incomplete anti-By antibody present in Mrs. M's serum would be classed as of natural occurrence. In July, 1960, Mrs. M. was delivered of her third baby which was group O By-negative, and normal. The maternal and cord sera both contained incomplete anti-By antibodies to an identical titre, when tested with By-positive red cells which had been stored in glucose-citrate solution for 12 months at 5° C. The By antigen is obviously a stable antigen.

References.

CAHAN, A., JACK, J. A., SCUDDER, J., SARGENT, M., SANGER, R., and RACE, R. R. (1957), "A Family in which A_x is Transmitted through a Person of the Blood Group A_2B", *Vox. Sang. (Basel)*, 2: 8.

CELANO, M. J., LEVINE, P., and LANGE, S. (1957), "Studies on Eluates from Rhesus and Human A_o Red Cells", *Vox. Sang. (Basel)*, 2: 375.

CLEGHORN, T. E. (1959), personal communication.

ENGELFRIED, J. J. (1955), "Another Instance of the Blood Subgroup A_o", *Amer. J. clin. Path.*, 25, 1326.

FISCHER, W., and HAHN, F. (1935), *"Über auffallende Schwäche der gruppenspezifischen Reaktionfähigkeit bei einem Erwachsenen", Ztschr. Immun.-Forsch.*, 84: 177.

GROVE-RASMUSSEN, M., SOUTTER, L., and LEVINE, P. (1952), "A New Subgroup (A_o) Identifiable with Group O Serums", *Amer. J. clin. Path.*, 22: 1157.

RACE, R. R., and SANGER, R. (1958), "Blood Groups in Man", Blackwell, Oxford.

SIMMONS, R. T., and WERE, S. O. M. (1955), "A 'New' Family Blood Group Antigen and Antibody (B_y) of Rare Occurrence", MED. J. AUST., 2: 55.

STRATTON, F., RENTON, P. H., and HANCOCK, J. A. (1958), "Red Cell Agglutinability Affected by Disease", *Nature (Lond.)*, 181: 62.

VAN LOGHEM, J. J., DORFMEIER, H., and VAN DER HART, M. (1957), "Two A Antigens with Abnormal Serologic Properties", *Vox. Sang (Basel)*, 2: 16.

WEINER, W., LEWIS, H. B. M., MOORES, P., SANGER, R., and RACE, R. R. (1957), "A Gene, *y*, Modifying the Blood Group Antigen A", *Vox. Sang. (Basel)*, 2: 25.

WIENER, A. S. (1953), "The Blood Factor C of the A-B-O System with Special Reference to the Rare Blood Factor C", *Ann. Eugen. (Lond.)*, 18: 1.

WIENER, A. S., and GORDON, E. B. (1956), "A Hitherto Undescribed Human Blood Group, A_m", *Brit. J. Hæmat.*, 2: 305.

WIENER, A. S., and WEXLER, I. B. (1958), "Heredity of the Blood Groups", Grune & Stratton, New York.

PREGNANEDIOL EXCRETION IN MULTIPLE PREGNANCY.

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IN our studies on patients who had suffered recurrent abortions, the pregnanediol excretion in the urine of a control series of normal pregnant women was found to vary over a wide range (Alder and Krieger, 1957). However, it was also shown that the majority of abortions occurred when the pregnanediol excretion fell to a critical level, whereas only a few abortions occurred when it was maintained above the average normal level (Rawlings and Krieger, 1958).

In the 1952-1954 series of patients studied because of recurrent abortion, one patient had an abortion of twins at 18 weeks. Her pregnanediol excretion was very low, but rose to the average normal level with corpus luteum treatment. Treatment was discontinued, but the normal pregnanediol excretion was maintained for four weeks. It then fell slightly during the next two weeks, uterine contractions commenced and abortion followed. These findings suggested that maintenance of the pregnanediol excretion at the average normal level established for pregnancies involving only one fœtus might not be adequate in cases of multiple pregnancy.

In the present paper, the previous history, the pregnanediol excretion and the result of 10 instances of multiple pregnancy are recorded. Nine of the mothers had twins and one had triplets. Eight cases emerged from our investigation of 460 cases of recurrent abortion, and two were especially included.

CASE I.—This patient had previously had a miscarriage at 27 weeks (1949), and abortions at nine weeks (1950), at seven weeks (1952) and at eight weeks (1953). In the present pregnancy, pregnanediol excretion was low at eight, nine and 10 weeks, but was raised to and maintained at the average normal level by exhibition of ethisterone (25 mg. per day) and injections of "Lutocyclin" (10 mg. three times per week) from the tenth to the twelfth week. Treatment then ceased. At 18 weeks the onset of uterine contractions (thought by the patient to be the result of taking an aperient) was followed by miscarriage of twin fœtuses (May, 1954).

CASE II.—Abortions had occurred at eight weeks (1953) and at 10 weeks (1953). In 1954, at six weeks of amenorrhœa, the patient was ordered 10 mg. of ethisterone per day. Pregnanediol excretion tests, commenced at 11 weeks, gave high figures, and continued to do so throughout the pregnancy. The hæmoglobin value was 86% (12·6 grammes per 100 ml.) at the beginning of pregnancy, but it gradually fell to 73% (10·8 grammes per 100 ml.) at 16 weeks despite oral iron therapy. At 18 weeks the patient was admitted to hospital with abdominal discomfort and slow blood loss per vaginam. She was given a transfusion of two pints of blood. The collection of a 24-hour specimen of urine was commenced at the same time as the blood transfusion was being given and whilst uterine contractions continued. Next day the cervix was fully dilated, and the patient had a miscarriage of twin fœtuses (October, 1954). The pregnanediol excretion level was high throughout.

CASE III.—After a full-term pregnancy in 1951, abortions occurred at 10 weeks (1952), at six weeks (1953) and at 12 weeks (1953). Seminal investigation of the father disclosed 44% of abnormal spermatozoa, which seemed to indicate a possible causative factor for the repeated abortions. Despite a premenstrual endometrial biopsy showing a rich secretory endometrium with decidual reaction, the patient was admitted to hospital with signs of threatened abortion at seven weeks of pregnancy. The pregnanediol excretion was maintained well above the normal average, and the pregnancy proceeded normally except for one episode of abdominal pain at 14 weeks, relieved by the exhibition of 20 mg. of ethisterone per day for three days. Tests ceased at 27 weeks. Twin pregnancy was diagnosed and confirmed at 32 weeks. The patient came into spontaneous labour at 36 weeks (February, 1955), and was delivered of live twins (a male weighing 5 lb. 12 oz. and a female weighing 5 lb.).

CASE IV.—This patient, a primigravida, was diagnosed at 30 weeks as having twins, and pregnanediol tests were immediately instituted. Only three assays were done, and the excretion was below the average normal in two of them. Premature labour occurred at 33·5 weeks, but the twin babies lived (April, 1955).

CASE V.—This patient had had prior miscarriages at three months (1951), at four months (1953) and at seven months (1954). The hæmoglobin value fell from 86% (12·6 grammes per 100 ml.) at nine weeks to 76% (11·3 grammes) at 13 weeks. She then had a loss of dark blood per vaginam and was given a transfusion of one pint of blood. Repeated small blood losses occurred, and the hæmoglobin value again fell from 93% (13·6 grammes per 100 ml.) to 73%

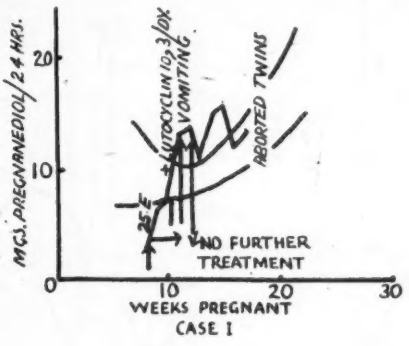

FIGURE I.

Case I. To show that normal average pregnanediol excretion appears insufficient to maintain a twin pregnancy to term.

(10·8 grammes). A transfusion of one pint of blood was given at 15 weeks. The blood loss now ceased, and as the pregnanediol excretion rose high above the average level, the patient was discharged from hospital two weeks later. Five days later she was readmitted to hospital complaining of recurrent abdominal pains. She had a quick miscarriage of twins, the first with its own placenta of low implantation, and 30 minutes later the second with its placenta. The specimen for the test at 21 weeks was collected on July 22, 1955, and miscarriage occurred on July 27. Pregnanediol excretion was well above the average normal on all occasions, although there was a sharp drop before the abortion occurred. The repeatedly failing hæmoglobin value and repeated vaginal losses of blood due to placenta prævia rather clouded the picture.

It is interesting to note that in the patient's next pregnancy, during 1956, no pregnanediol tests were done because of the high level of excretion in the previous pregnancy. This pregnancy proceeded satisfactorily, with the size of the uterus corresponding to the period of amenorrhœa until at 32 weeks the patient suddenly went into premature labour and was delivered of a live male child weighing 3 lb. 5 oz. and a fœtus papyraceus.

CASE VI.—This patient had had (i) an abortion at seven weeks (1946), (ii) a full-term living baby which weighed 7·5 lb. (1947), (iii) an abortion at seven weeks and a miscarriage at 15 weeks in 1948, (iv) a living baby after lower segment Cæsarean section at 36 weeks in a pregnancy complicated by placenta prævia and repeated blood losses (1949), and (v) a miscarriage at 14 weeks with "shows" from nine to 11 weeks (1953).

A pregnancy test at eight weeks gave a positive result, and she was given ethisterone (10 mg. per day). The pregnanediol excretion was above the average normal and became very high from 26 to 28 weeks, after which tests ceased. Twin babies weighing 5 lb. 4 oz. and 6 lb. respectively were delivered three days before term (December, 1955).

CASE VII.—This patient had a curious obstetrical history. She had mild hypertension throughout her first pregnancy, which resulted in a full-term living baby weighing 4 lb.

15 oz. In the next two pregnancies mild hypertension was again present. At 36 and 38 weeks respectively she had sudden and apparently causeless attacks of diarrhœa. In both pregnancies death in utero and delivery of small stillborn babies followed immediately after these episodes. In her fourth pregnancy hyperpiesis responded to "Serpasil". The graph of pregnanediol excretion showed two low episodes at 20 and 33 weeks. Because of a low hæmoglobin value, blood transfusions were required at 18 and 24 weeks. At 36 weeks the patient reported the onset of vomiting and diarrhœa. The membranes were artificially ruptured immediately, and a living baby which weighed 4 lb. 1 oz. was born. In the fifth pregnancy the pregnanediol excretion was very low (just above the critical level for seven weeks). At 14 weeks it rose to the average normal value. Ethisterone therapy ceased at 20 weeks, and the

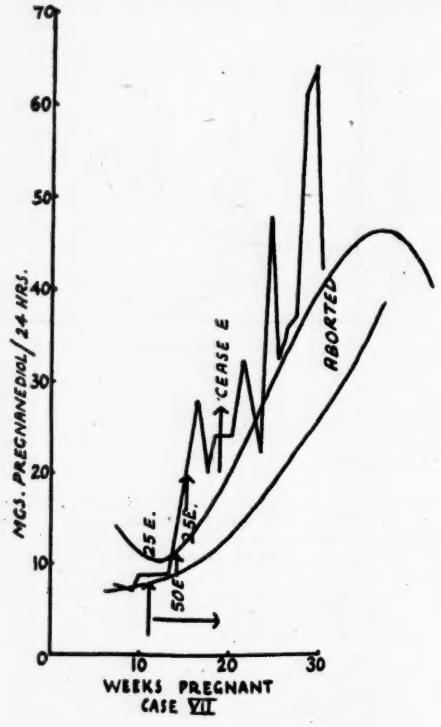

FIGURE II.

Case VII. To illustrate the same point as in Figure I, and also to show the typical sharp fall that precedes abortion.

pregnanediol excretion remained above the average normal till 30 weeks. X-ray examination at 27 weeks confirmed the presence of twin pregnancy. As a further test we decided not to resume supplemental ethisterone therapy. At 30 weeks, after the patient had experienced a feeling of pressure, the membranes ruptured, and two days later the patient was delivered of live twins. It is interesting to note the sharp fall in pregnanediol excretion from 64 mg. to 42 mg. two days before delivery. This last specimen was collected during the 24 hours following spontaneous rupture of the membranes (November, 1956).

CASE VIII.—This patient had had a full-term pregnancy in 1951, followed by miscarriages at 13, 18 and 21 weeks and an abortion at seven weeks. In the present pregnancy, the patient expressed doubts about a successful outcome. At eight weeks the uterus was equal in size to a 12 weeks' pregnancy, but the result of the Aschheim-Zondek test was negative. At 14 weeks the uterus was almost at the level of the umbilicus. Pregnanediol tests were commenced and the excretion was very high. The family history of the patient's mother being a twin and a sister having conceived twins supplied the obvious diagnosis. The patient was given depot "Proluton" (125 mg. biweekly) and ethisterone (30 mg. per day) until 19 weeks, when X-ray examination confirmed the presence of a twin pregnancy. In view of our theory that high pregnanediol excretion was desirable in twin pregnancies the dosage of ethisterone was increased to 50 mg. per day. The hæmoglobin value was 76% (11 grammes per 100 ml.) at nine weeks, but only 66% (9·4 grammes) at 23 weeks despite oral iron therapy and 30 ml. of

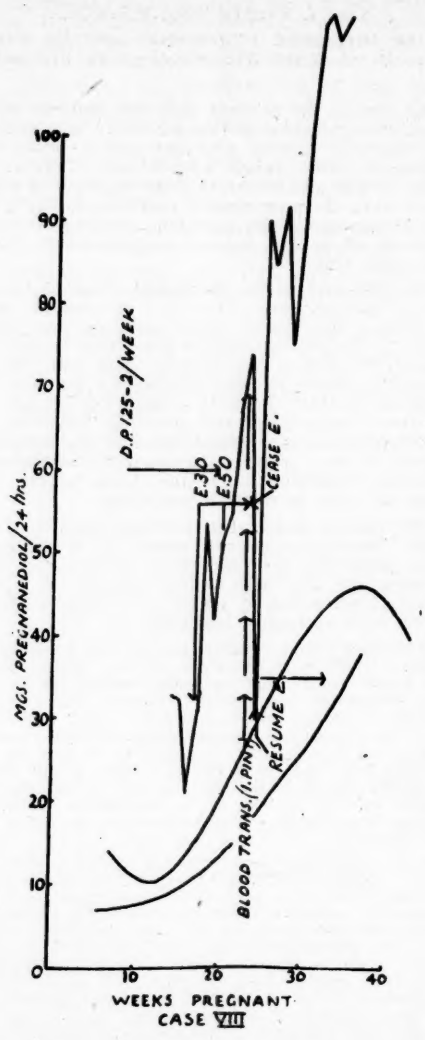

FIGURE III.

Case VIII. To illustrate the value of maintaining high pregnanediol excretion; the pregnancy went on to term.

"Imferon" given intramuscularly. A transfusion of three pints of blood raised the hæmoglobin value to 86% (12·5 grammes per 100 ml.), and progesterone therapy ceased. The pregnanediol excretion immediately fell, but rose on the resumption of a dosage of 50 mg. of ethisterone per day. The pregnancy continued uneventfully until term, when the patient gave birth to living twins weighing 7 lb. 15 oz. and 6 lb. 6 oz. respectively (November, 1958).

CASE IX.—In the first pregnancy of this patient, X-ray investigation at 29 weeks revealed the presence of triplets. Pregnanediol excretion at 31 weeks was 109 mg. (normal average 42·2 mg), and at 32 weeks it was 176 mg. She came into labour spontaneously at 32·5 weeks (November, 1958). The babies weighed 3 lb. 15 oz., 4 lb. 1 oz. and 3 lb.

6 oz. respectively, and all survived. This was a case of triovular triplets.

CASE X.—During her first marriage, this patient had had miscarriages at 14 weeks (1951) and 12 weeks (1952), and an abortion at 10 weeks (1953). In her second marriage, miscarriages occurred at 22 weeks (1956) and 24 weeks (1957). In the present pregnancy the Aschheim-Zondek test gave a negative result at eight weeks of amenorrhœa, but a positive result at nine weeks. From nine and a half weeks the patient received injections of 50 mg. of progesterone per day. Since the pregnanediol excretion was well above the average normal the dosage was reduced to 25 mg. per day and then to 50 mg. three times per week, as the patient was living in the country and the visiting nurse lived some distance away. However, since pregnanediol excretion fell to a critical level at 15 weeks, the dose of progesterone was increased to 25 mg. per day. The excretion rose to above the average normal figure at 17 weeks, and then fell to just below the average normal at 19 weeks; miscarriage of twins occurred during the next week. In this case the pregnanediol excretion level was not maintained well above the average normal level.

Discussion.

The unexpected miscarriage of the first patient, whose pregnanediol excretion curve was at the average normal level found in patients with single pregnancies, raised the question as to whether a higher blood level of progesterone and consequently a higher level of pregnanediol excretion should be present for multiple pregnancy to be successful. The very high levels of pregnanediol excretion in the second case seemed to confirm this view. This pregnancy terminated at 18 weeks, but the miscarriage was probably due to the falling hæmoglobin value, which failed to respond to oral iron therapy. Blood transfusion given whilst uterine contractions were occurring failed to avert miscarriage.

The third and fifth patients both had high pregnanediol excretion curves. The pregnancy of the former proceeded to 36 weeks, whilst that of the latter terminated by miscarriage at 22 weeks. However, the picture was obscured in this case by placenta prævia in relation to the first twin.

In Case IV, pregnanediol excretion was below average normal, and premature labour occurred at 33·5 weeks.

In the sixth and eighth cases, a high level of pregnanediol excretion was maintained by exhibition of ethisterone. Both pregnancies continued to term, with the birth of living twins. In the eighth case, the low hæmoglobin value at 23 weeks had to be adjusted by blood transfusion. This case showed the desirability of high pregnanediol excretion and normal hæmoglobin value. The withholding of progesterone derivatives at 30 weeks in Case VII was immediately followed by a marked fall in pregnanediol excretion, and then premature labour occurred. This case confirms the idea that a high pregnanediol excretion is necessary if the pregnancy is to continue to term.

The ninth patient had a premature labour at 30 weeks, in spite of very high excretion of pregnanediol at 29 and 30 weeks. However, distension due to triplets introduced a mechanical factor which resulted in premature labour. All the babies were born alive.

In Case X, early miscarriage occurred. Because of difficulty due to distance and monetary factors, it was impossible for the patient to be given sufficient corpus luteum therapy to maintain a high pregnanediol excretion. Prophylactic ligature of the cervix might have been helpful in this instance.

The number of cases of multiple pregnancy studied is far too small to allow significant conclusions to be drawn; but the following comparison suggests the desirability of maintaining a high level of pregnanediol excretion. Among four patients with lower levels of pregnanediol excretion there were two miscarriages and two premature labours at 30 and 33·5 weeks respectively. Among the six patients with high levels, one pregnancy terminated at 36 weeks, two pregnancies proceeded to term, one premature labour was associated with the birth of triplets at 32·5 weeks and two miscarriages occurred. Both of the patients who had miscarriages had low hæmoglobin values, and one had placenta prævia.

The high incidence of twins in a series of patients selected for study only because of a history of recurrent abortion is also interesting. Eight twin pregnancies occurred in the 460 studied, whereas the incidence of twins is usually regarded as about 1 in 85—that is, 8 in 680.

Summary.

1. A study of the pregnanediol excretion of 10 patients with multiple pregnancies suggests that a higher blood level of progesterone than that adequate for a single fœtus is necessary for the pregnancy to proceed to term.

2. When abortion or miscarriage occurred, the pregnanediol excretion was near the average normal level for a pregnancy with a single fœtus, or there was a marked fall from a higher level.

3. Premature labour sometimes occurred even when the pregnanediol excretion level was high probably owing to the mechanical factor of the combined weights of the babies.

Acknowledgements.

We wish to thank the members of the honorary medical staff of the Royal Women's Hospital, Melbourne, for the use of clinical material, the Biochemistry Section for technical assistance, and Miss M. Johnson for the preparation of the graphs.

References.

ALDER, R. M., and KRIEGER, V. I. (1957), "Hormonal Therapy and the Significance of the Pregnanediol Test in Recurrent Abortion", MED. J. AUST., 2: 122.

RAWLINGS, W. J., and KRIEGER, V. I. (1958), "Studies in the Prevention of Recurrent Abortion Due to Corpus Luteum Deficiency", MED. J. AUST., 2: 561.

Addendum.

Since this paper was submitted for publication, Shearman's[1] article stating that "there is no significant difference in the excretion of pregnanediol in twin pregnancy when compared to single pregnancy" has been published. A possible explanation for the difference between his conclusion and our own may be the fact that his investigations were carried out only over the period of 33 to 40 weeks, whereas our patients were studied throughout pregnancy.

AUTOANTIBODY TESTS IN THYROID DISEASE.

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THE boundaries, both clinical and pathological, dividing Hashimoto's disease, Riedel's struma and subacute thyroiditis of de Quervain have always been indistinct. Histological examination of the gland in primary myxœdema shows changes which are of the same nature as those in Hashimoto's disease, but usually are not nearly so extensive. There is a distinct difference in the frequency with which the various types of thyroiditis are diagnosed in different places — a difference, it is suspected, due as much to the prevailing local criteria of diagnosis as to a difference in incidence.

Further difficulty in the diagnosis of thyroid disease is due to the poor correlation between structural and functional changes. A complete diagnosis requires multiple laboratory tests of thyroid function, serum protein and flocculation studies, and histological examination of sections in many cases.

Since Roitt and Doniach's (1956) work, several serological tests have been applied for the detection of circulating antibodies reacting with components of the

[1] Shearman, R. P. (1959), "Pregnanediol Excretion in Pregnancy", *J. Obstet. Gynæc. Brit. Emp.*, 66: 1, 11.

thyroid gland. Adequate data have now accumulated to allow evaluation of the significance of these tests, both as to their usefulness to the clinician and as to the contribution they have made to the understanding of the disease processes of the thyroid gland. In elaborating the present opinions it is as well to consider what was originally expected of these tests.

The discovery of precipitating antibodies by the technique of agar gel diffusion was at first construed as evidence that Hashimoto's disease was the result of an antibody-antigen interaction taking place in the thyroid. It was hoped that gel precipitation techniques would enable an unequivocal diagnosis of Hashimoto's disease to be made. A single reliable diagnostic test is of value in any field, but would be particularly so here, for the concept of Hashimoto's disease lacks clinical precision. Even the histological appearances are interpreted by different pathologists in widely different ways. Unfortunately it soon became apparent that the new test had limited practical application because of its failure to discriminate properly between Hashimoto's disease and other types of thyroid disease, at any rate according to our present diagnostic categories.

The agar gel diffusion technique showed positive results not only in Hashimoto's disease but in cases of primary myxœdema, a condition in which an autoimmune pathogenesis was unsuspected. The tanned red-cell hæmagglutination technique of Boyden (1951) then proved to be more delicate, and by its use thyroglobulin antibodies were demonstrated in a much higher percentage of cases of primary myxœdema and also in a high percentage of cases of thyrotoxicosis.

Techniques Used to Demonstrate Thyroid Antibodies.

The following seven tests are used to demonstrate thyroid antibodies.

Agar Gel Diffusion.

Precipitating antibodies are demonstrated by this technique, which depends on a solution of thyroglobulin (or thyroid extract) and serum containing thyroglobulin antibody diffusing in opposite directions through agar; precipitation occurs where antigen and antibody meet in optimum proportions.

In approximately 70% of cases of Hashimoto's disease positive results are obtained, but in only 20% of cases of myxœdema. In other thyroid diseases the proportions of sera giving positive reactions are very small. For example, in Roitt and Doniach's (1958) series, in only one of 198 cases of non-toxic nodular goitre tested was a positive result obtained, and in two of 181 cases of thyrotoxicosis. From the clinician's point of view, as a diagnostic test this method is useful, but will not reveal 30% of cases of Hashimoto's disease, and in 20% of cases of myxœdema the result of the test is positive.

Tanned Cell Hæmagglutination.

Tanned cell hæmagglutination is carried out by taking tannic acid treated red cells which have been coated with thyroglobulin or thyroid extract and mixing them with the serum to be tested. If antibodies are present, agglutination occurs through linkage of the cells by antibody molecules.

With this technique, a high percentage of positive reactions occurs in Hashimoto's disease (91%, Roitt and Doniach, 1958) and in myxœdema (81%, Owen and Smart, 1958). However, a high percentage of positive results is gained at the expense of specificity, for in 36% of cases of thyrotoxicosis (Blizzard *et alii*, 1959) and in 27% of cases of non-toxic nodular goitre (Roitt and Doniach, 1958) a positive reaction is obtained. In significant proportions of other diseases (including thyroid carcinoma) the results are also positive.

"False positive" reactions have been obtained in control sera — that is, from patients apparently without thyroid disease — by several groups of workers using the technique (see Table I). Blizzard *et alii* (1959) found 4%, Roitt and Doniach (1958) 5%, and Owen and Smart (1958) 6%. Hackett, Beech and Forbes (1960*a*) have found higher percentages than these. Positive reactions were obtained in 9% of blood donors and in 18% of hospital patients with a wide variety of diseases, whose thyroid was clinically unaffected. No particular pattern of disease was found in a study of these patients whose sera gave anomalous positive reactions.

Complement Fixation Test with Thyrotoxic Antigen.

Similar over-all results are obtained with this technique to those obtained with the tanned cell hæmagglutination technique, but the correlation is not complete. Roitt and Doniach (1958) showed a reasonable agreement between the results of the tests in Hashimoto's disease, but a considerable discrepancy in myxœdema and thyrotoxicosis. Positive results are obtained with roughly similar frequency in these conditions, but sera from many cases react positively in only one of the two tests. "False positive" reactions occur not infrequently with this technique. Goudie, Anderson and Gray (1959), testing sera of 486 hospital patients without clinical evidence of thyroid disease by the complement fixation (toxic thyroid) test, found 6·8% of positive results. Of 143 of these sera, coming from women aged over 60 years, 16% reacted positively. A positive reaction in life was correlated with mild Hashimoto-like changes at autopsy. However, several glands showing this change at autopsy came from patients whose serum failed to react during life.

Complement Fixation Test with Normal Thyroid Antigen.

Hackett, Beech and Forbes (1960*b*) have performed this test on thyroid disease serum, and on 947 sera from patients without thyroid disease. Four out of 10 patients with myxœdema (some of whom had a firm goitre and other criteria of Hashimoto's disease) reacted positively, as did five of 16 with thyrotoxicosis and three of 16 with euthyroid goitre. Sera of 10% of the 947 mixed hospital medical patients gave positive results. Serum from only four of 101 blood donors reacted. This test therefore shows only a mild correlation with clinical disease of the thyroid, and is obviously of no value in clinical medicine, although it is an intriguing phenomenon in serological research. The test is similar to the Wassermann tests, and results with it are just as reproducible, but, like the Wassermann test, it is poorly understood. It has been stated that the factor responsible for complement fixation in this test is the same as the thyrotoxic complement-fixing factor, the difference being merely one of concentration of the antigen (Roitt and Doniach, 1958). This is quite unproven and is probably not the case (Hackett *et alii*, 1960*b*). If they are separate factors, they are nevertheless almost certainly present together in toxic thyroid glands, and the non-toxic factor probably fixes complement with certain sera with which the toxic factor does not react. It may therefore be responsible for some of the so-called "false positive" reactions in which complement fixation occurs in the absence of thyroid disease. Sera reacting with normal thyroid antigen usually fix complement with extracts of other tissues — lung, liver, adrenal or kidney.

Cutaneous Sensitivity Test.

Cutaneous sensitivity to thyroid extracts probably demonstrates the presence of circulating antibodies or reagins. Buchanan *et alii* (1958) used a skin test which gave a weal maximal at 24 hours when unheated thyroid gland antigen was injected intradermally into patients whose sera was found to contain precipitins by the agar gel technique. This test cannot be used widely because of the risk of transmitting viruses.

Passive Cutaneous Anaphylaxis.

The test for passive cutaneous anaphylaxis (Ovary *et alii*, 1958) is carried out in experimental animals. Serum is injected subcutaneously, and after three to five hours

TABLE I.

Authors.	Clinical State.	Number.	Positive Result to Precipitin Test.	Tanned Cell Hæmagglutination Positive Results.	Complement Fixation Test: Positive Results.	
					Toxic Thyroid.	Normal Thyroid.
Roitt and Doniach (1958)	Hashimoto's disease	106	71 (67%)	96 (91%)	96 (91%)	—
	Myxœdema	101	19 (19%)	66 (65%)	64 (63%)	—
	Thyrotoxicosis	181	2 (1%)	103 (57%)	67 (37%)	—
	Euthyroid goitre	198	1 (0·5%)	54 (27%)	17 (9%)	—
Owen and Smart (1958)	Hashimoto's disease:					
	Recent	34	—	29 (85%)	—	—
	Long-standing	43	—	33 (77%)	—	—
	Myxœdema	78	—	63 (81%)	—	—
Cline *et alii* (1959)	Hashimoto's disease	16	—	14 (88%)	—	—
Blizzard *et alii* (1959)	Myxœdema	10	—	7 (70%)	—	—
	Thyrotoxicosis	94	—	34 (36%)	—	—
	Euthyroid goitre	19	—	8 (42%)	—	—
Belyavin and Trotter (1959)	Hashimoto's disease	64	27 (42%)	—	51 (80%)	—
	Myxœdema	19	4 (21%)	—	10 (53%)	—
	Thyrotoxicosis	66	6 (9%)	—	28 (42%)	—
	Euthyroid goitre	33	0	—	4 (12%)	—
Anderson, Goudie and Gray (1959*b*)	*Hashimoto's disease*	*60*	42 (70%)	—	52 (87%)	—
	Myxœdema	90	13 (14%)	—	48 (53%)	—
	Thyrotoxicosis	247	5 (2%)	—	128 (52%)	—
	Euthyroid goitre	44	—	—	4 (9%)	—
Hackett, Beech and Forbes (1960*a*)	Hashimoto's disease	8	—	6 (75%)	—	—
	Myxœdema	20	—	14 (70%)	—	7 (37%)
	Thyrotoxicosis	23	—	13 (57%)	—	6 (26%)
	Euthyroid goitre	16	—	7 (44%)	—	3 (23%)
Hackett, Beech and Forbes (1960*b*)	Hashimoto's disease and myxœdema	10	—	—	5 (50%)	4 (40%)
	Thyrotoxicosis	16	—	—	12 (75%)	5 (31%)
	Euthyroid goitre	13	—	—	7 (54%)	3 (23%)
Roitt and Doniach (1958)	Control	195	—	—	0	—
	Control	146	—	8 (5%)	—	—
Owen and Smart (1958)	Control	*52*	—	*3 (6%)*	—	—
Blizzard *et alii* (1959)	Control	219	—	8 (4%)	—	—
Goudie *et alii* (1957)	Control	133	0	—	—	—
Goudie, Anderson and Gray (1959)	Control	486	—	—	33 (6·8%	—
Belyavin and Trotter (1959)	Control	36	0	—	2 (6%)	—
Hackett, Beech and Forbes (1960*a*, 1960*b*)	Mixed medical conditions	387	—	68 (18%)	—	—
	Normal—blood donors	101	—	9 (9%)	10 (10%)	4 (4%)
	Mixed medical conditions	947	—	—	—	99 (10%)

the antigen solution, together with a blue dye to outline the site of increased capillary permeability, is injected intravenously. A blue spot indicates an antibody-antigen reaction. (This test is similar in principle to that of Buchanan *et alii*, 1958.)

Pulvertaft *et alii* (1959) have recently published preliminary work on the use of unheated sera in thyroid tissue cultures. Inhibitory and cytotoxic effects were obtained with several Hashimoto sera. This work may solve many problems in the future, but at present it has not been established whether the inhibitory effects are due to antibodies of a different type or to another cytotoxic agent.

The Nature of Thyroid Autoantibody Reactions.

As thyroid autoantibodies are frequently detected in persons in whom there is no clinical evidence of thyroid disorder, and as they occur in high frequency in diverse diseases of the gland, the phenomenon is not simply explained. Characterization of the antigens and antibodies reacting *in vitro* may clarify the position. The present views on their nature may be summarized briefly.

1. Three antigens seem to be playing a part, as follows. (*a*) The first is thyroglobulin, which reacts with a precipitating antibody in agar gel tests. The same antigen-antibody system is apparently involved in hæmagglutination tests (Anderson, Goudie and Gray, 1959*a*). Some Hashimoto sera react by complement fixation with thyroglobulin (Anderson, Goudie and Gray, 1959*a*; Belyavin and Trotter, 1959), but not the majority (Roitt and Doniach, 1958). (*b*) A distinct antigen is present in toxic thyroid glands and is located in the microsomal fraction of the cells (Belyavin and Trotter, 1959). It fixes complement with an antibody which is separable from the precipitin responsible for agar gel and tanned cell hæmagglutination reactions. (*c*) Complement fixation (normal thyroid) probably depends on a separate antigen (Hackett, Beech and Forbes, 1960*b*), which is also present in toxic glands and complicates the results of the complement fixation (toxic thyroid) test. Sera reacting with normal thyroid extract usually fix complement with extracts from other human tissues (Hackett, Beech and Forbes, 1960*b*).

2. The antibodies involved are therefore: (*a*) the precipitin type antibody reacting with thyroglobulin in agar gel and hæmagglutination reactions; (*b*) a complement-fixing thyroglobulin antibody (this may be the same as (*a*)—Belyavin and Trotter, 1959); (*c*) a complement-fixing antibody reacting with a microsomal antigen in toxic thyroid glands; (*d*) a complement-fixing antibody reacting with a cellular antigen in normal and toxic thyroid glands.

These factors have been recognized so far; there may well be more. Pulvertaft *et alii* (1959) have demonstrated a toxic factor in unheated serum. Roitt and Doniach (1958) obtained precipitin reactions in some sera which gave very low titres by tanned cell hæmagglutination; the latter reactions are generally thought to depend on the same antibody.

It now seems quite clear that the antibodies which can be demonstrated *in vitro* are not damaging to the gland. It may well be that they are merely a reflection of the presence of lymphocytes and plasma cells which, bearing cell-bound antibodies, actually cause damage to the gland. This awaits proof. However, it is certain that the reticuloendothelial system is involved. The presence of antibodies in the blood correlates fairly well with the finding of lymphocytes and plasma cells in the gland (Roitt and Doniach, 1958; Goudie, Anderson and Gray, 1959*b*).

Autoantibodies may arise when components of the thyroid (particularly thyroglobulin) come in contact with antibody-forming cells for the first time. Normally the contents of the acini, like lens tissue and spermatozoa, are separated by membranous barriers from the reticuloendothelial system, and the formation of antibodies may merely indicate the violation of this sanctity at some time in the past. A positive result to the tanned cell hæmagglutination test may in fact have a similar significance to that of the Mantoux test, being merely an indication of past disease, not necessarily active. If this is the case, autoantibody studies may not have advanced

knowledge of the ætiology of thyroid disease, although they may ultimately show that an immunological mechanism modifies the course of some thyroid diseases.

There may be many causes of damage to the gland. Virus infection, particularly mumps, is one (Eylan, Zmucky and Sheba, 1957; Felix Davies, 1958). The high incidence of autoantibodies found in thyrotoxicosis indicates that pituitary stimulation may be another.

Autoantibody studies favour a unified concept of Hashimoto's disease and primary myxœdema, which are immunologically (by current tests) similar, the only difference being greater average titre in the former (Owen and Smart, 1958).

The Value of Thyroid Antibody Tests to the Clinician.

The lack of correlation of the serological findings with the clinical state of the thyroid renders these tests of little value to the clinician at present. The possibility remains that a positive result may in the future indicate a specific treatment, if the criteria for diagnosis of thyroid disease are advanced sufficiently to show that a positive reaction does in fact mean that thyroid disease is present.

There is no value in carrying out tanned cell hæmagglutination tests in cases of goitre, since a positive reaction is obtained frequently even in the case of simple goitre (approximately one-third of patients react). The height of the titre is of no value in the individual case, for high titres are found in occasional cases of simple goitre.

Tanned cell hæmagglutination tests are of no value in the diagnosis of Hashimoto's disease for the same reason; the same applies to the complement fixation (toxic thyroid) test. Precipitin tests, because of their relative insensitivity, are of more value. The fact that they give positive results in 20% of cases of primary myxœdema matters little if these two conditions are accepted as being variations of the same process. However, in 30% of cases of lymphadenoid goitre acceptable by other criteria, the results of precipitin tests are negative.

Tanned cell hæmagglutination and complement fixation (toxic thyroid) tests are of limited value in the diagnosis of myxœdema because of the frequency of "false positive" reactions, particularly in elderly females, in regard to whom diagnostic help is most frequently required. Diagnosis must still be confirmed by conventional methods; it is not justifiable to treat a patient merely on the basis of a positive response to an antibody test. Therefore, autoantibody tests offer little to the clinician seeking help in the diagnosis of thyroid disease. The most valuable is the precipitin test; if the result is positive, it indicates that the patient has Hashimoto's disease or primary myxœdema. These are now generally agreed to be caused by the same process.

Summary.

The tests for thyroid autoantibodies and results obtained with them are discussed.

These tests probably indicate leakage of the contents of thyroid follicles as a result of damage in the past, and so frequently produce positive results that they are of little help in the diagnosis of thyroid disease.

The precipitin test, because of its relative insensitivity, is of most value. If the result is positive, it indicates that the patient has Hashimoto's disease or primary myxœdema. These are probably manifestations of the same disease process.

Acknowledgement.

I thank Professor H. N. Robson for his help in the preparation of this paper.

References.

Anderson, J. R., Goudie, R. B., and Gray, K. G. (1959a), "Complement-Fixing Autoantibody to Thyroglobulin in Hashimoto's Disease", *Lancet*, 1: 644.

Anderson, J. R., Goudie, R. B., and Gray, K. G. (1959b), "The 'Thyrotoxic' Complement-Fixation Reaction", *Scot. med. J.*, 4: 64.

Belyavin, G., and Trotter, W. R. (1959), "Investigations of Thyroid Antigens Reacting with Hashimoto Sera. Evidence for an Antigen other than Thyroglobulin", *Lancet*, 1: 648.

Blizzard, R. M., Hamwi, G. J., Skillman, T. G., and Wheeler, W. E. (1959), "Thyroglobulin Antibodies in Multiple Thyroid Disease", *New Engl. J. Med.*, 260: 112.

Boyden, S. V. (1951), "The Adsorption of Protein on Erythrocytes Treated with Tannic Acid and Subsequent Hemagglutination by Antiprotein Sera", *J. exp. Med.*, 93: 107.

Buchanan, W. W., Anderson, J. R., Goudie, R. B., and Gray, K. G. (1958), "A Skin Test in Thyroid Disease", *Lancet*, 2: 928.

Cline, M. J., Selenkow, H. A., and Brooke, M. S. (1959), "Autoimmunity in Thyroid Disease", *New Engl. J. Med.*, 260: 117.

Eylan, E., Zmucky, R., and Sheba, C. (1957), "Mumps Virus and Subacute Thyroiditis", *Lancet*, 1: 1062.

Felix-Davies, D. (1958), "Autoimmunization in Subacute Thyroiditis Associated with Evidence of Infection by Mumps Virus", *Lancet*, 1: 880.

Goudie, R. B., Anderson, J. R., and Gray, K. G. (1959), "Complement-Fixing Antithyroid Antibodies in Hospital Patients with Asymptomatic Thyroid Lesions", *J. Path. Bact.*, 77: 389.

Goudie, R. B., Anderson, J. R., Gray, K. G., Clark, D. H., Murray, I. P. C., and McNicol, G. P. (1957), "Precipitin Tests in Thyroid Disease", *Lancet*, 2: 976.

Hackett, E., Beech, M. D., and Forbes, I. J. (1960a), "Thyroglobulin Antibodies in Patients Without Clinical Disease of the Thyroid Gland".

Hackett, E., Beech, M. D., and Forbes, I. J. (1960b), "Complement Fixation with Extract of Normal Thyroid Gland: Its Occurrence in Sera from Patients with Thyroid Disease and in Other Conditions", *Aust. Ann. Med.*, 9: 93.

Ovary, Z., Randall, H., Witebsky, E., Rose, N. R., Shulman, S., and Metzgar, R. (1958), "Thyroid-Specific Autoantibodies Studied by Passive Cutaneous Anaphylaxis of Guinea Pig", *Proc. Soc. exp. Biol., Med.*, 99: 397.

Owen, S. G., and Smart, G. A. (1958), "Thyroid Antibodies in Myxœdema", *Lancet*, 2: 1034.

Pulvertaft, R. J. V., Doniach, D., Roitt, I. M., and Hudson, R. V. (1959), "Cytotoxic Effects of Hashimoto Serum on Human Thyroid Cells in Tissue Culture", *Lancet*, 2: 214.

Roitt, I. M., and Doniach, D. (1958), "Human Auto-Immune Thyroiditis:: Serological Studies", *Lancet*, 2: 1027.

Roitt, I. M., Doniach, D., Campbell, P. N., and Hudson, R. V. (1956), "Autoantibodies in Hashimoto's Disease (Lymphadenoid Goitre)", *Lancet*, 2: 820.

Rose, N. R., and Witebsky, E. (1956), "Studies on Organ Specificity. V: Changes in the Thyroid Glands of Rabbits Following Active Immunization with Rabbit Thyroid Extracts", *J. Immunol.*, 76: 417.

Reviews.

Biological Problems of Grafting. A Symposium sponsored by the Commission Administrative Du Patrimoine Universitaire de Liège and the Council for International Organizations of Medical Sciences; 1959. Oxford: Blackwell Scientific Publications Ltd. 9½" x 6", pp. 466, with illustrations. Price: 50s.

This volume contains the proceedings of a symposium on the biological problems of grafting sponsored jointly by the University of Liège and the Council for International Organizations of Medical Sciences (C.I.O.M.S.).

If the report of the deliberations of any gathering convened to discuss topics that are on the advancing edge of knowledge is to be of any real value to its readers, the interval which is allowed to elapse between the presentation of the material and its publication must be a very short one. The editors of this volume can claim, in this regard, to have done rather well, for the meeting was held late in March, 1959, and we are told on the title page that it was first published in July of that year. It is, then, all the more regrettable that the English translations (if translations they are) are often so inadequate, and that in the volumes supplied to us pages 53 to 84 were missing and as consolation we had pages 85 to 116 appearing twice.

But the apparent shortcoming of the binder can be forgiven, for the volume is an immensely valuable one to all workers busily engaged in the problem of tissue grafting, and of these there are now a great many. It is primarily for the expert, or certainly for one who has some familiarity with this kind of work and is acquainted with the relevant vocabulary.

The symposium enjoyed having as its chairman P. B. Medawar, and its deliberations were mainly concerned with a close examination of observed facts and of hypotheses relating to some of the fundamental problems which must be solved before we can claim to have the slightest understanding of the phenomena that are observed, for example, during the homograft reaction and in secondary disease. This emphasis on the fundamental aspects of tissue transplantation is, at the present state of our knowledge, a right and proper one. However, at the same time, room has been found for the practical application of the lessons which are being learned from the experimental biologist. One of the most interesting contributions of this latter kind is that by Dr. Mathé, which includes very valuable information on the technique of bone-marrow grafting.

The panel of contributors is an international one and includes most of the leading figures in this field. Not only are their contributions recorded in full, but there is a verbatim account of the informative discussion that followed each paper.

As we have said, this book is in the main one for the expert; it is a "must" for anyone engaged in the academic pursuit of medical knowledge. But the ordinary reader need not be reluctant to lift it down from the shelf, for he will find, if he picks and chooses a little, a great deal which is easy to read and easy to understand, and which will give him an authentic account of some of the exciting new developments in this kind of work.

Family Medical Costs and Voluntary Health Insurance: A Nationwide Survey. By Odin W. Anderson, Ph.D., and Jacob J. Feldman; 1956. New York, London, Toronto: McGraw-Hill Book Company, Incorporated. 9¼" × 6¼", pp. 270, with many tables. Price: $6.50.

VOLUNTARY INSURANCE with Government subsidy is the principle underlying the Australian National Health Service. Therefore any objective study of voluntary health insurance in operation must be of interest to those responsible, including the doctors who give the service and those who help to direct some of the insurance funds for the Australian scheme. The present book is such a study. For meticulous thoroughness, it could scarcely be excelled.

The authors rightly went to the source—namely, the homes of carefully selected samples of American families—and from there as starting point found the health costs of the average family and, through intimate study of the plans of voluntary insurance organizations, the extent to which those costs could be and were being met by insurance. To those interested in the working of a voluntary health insurance plan, this work is fascinating in its detail.

In the United States, the business of selling voluntary insurance is an intense one, between Blue Cross and Blue Shield plans on the one hand and insurance companies on the other. This has led to the employment of differential rates according to the risk of insuring a particular class. This in its turn necessitates regular study of the whole mechanism, such as the publication under review embodies.

Those familiar with the Australian scheme will be glad that the Commonwealth, in subsidizing plans based on uniform contributions, has enabled the insurance funds to maintain comparative simplicity in operation. Administrators of hospital and medical insurance funds in Australia will appreciate the proofs provided in this publication of the complexities involved in expense rating as opposed to uniform rating. This is a book that should be read by all medical insurance administrators.

Peripheral Nerve Injuries. By Ruth E. M. Bowden, D.Sc., M.B., B.S., L.R.C.P., M.R.C.S.; 1958. London: H. K. Lewis and Company, Limited. 7¾" × 4¾", pp. 68, with 30 illustrations. Price: 8s. 6d. (English).

THIS little book contains an immense amount of information, and is without doubt the most succinct account of nerve injuries yet published. Although it has been primarily written for medical students and physiotherapists, its 57 pages contain practically all that a surgeon needs to know about the subject. Free of complex experimental data, the text gives a lucid account of the type of nerve damage, diagnosis, assessment of prognosis and treatment. In diagnosis, careful history-taking and clinical examination are emphasized, although detailed methods of muscle testing are omitted. One is reminded of the pitfalls of sensory testing, chief among which are anatomical variations and the asking of leading questions. Electrodiagnosis, including electrical stimulation and electromyography, is discussed more briefly, and is regarded as an aid to diagnosis or a useful tool for research. An excellent chapter on anatomy summarizes the anatomical features which are of value in localizing and treating peripheral nerve lesions. The author gives warning of the risks to peripheral nerves from the use of tourniquets, plaster casts, injections and certain postures. Painful neuromata may be a problem in some amputation stumps, but it is doubtful whether many surgeons would agree with the author's advice to inject the cut end of a nerve with aqueous gentian violet solution or bury it in bone. Although a consideration of the finer points in surgical technique is necessarily omitted in a work of this type, it was rather surprising to find the author perpetuating the traditional dogmatic assertion that primary suture of a severed nerve is not the treatment of choice. While this may well apply to injuries treated initially by the unskilled, there is evidence that better results are achieved by experienced surgeons when definitive repair is undertaken at the first operation. However, the section on treatment is generally well done and pays particular attention to conservative methods. Professor Bowden, well known for her work on nerve injuries during the war and a contributor to the authoritative Medical Research Council pamphlet on the subject, is to be congratulated on a work which deserves to be widely read.

The Medical Assistant: A Guidebook for the Nurse, Secretary, and Technician in the Doctor's Office. By Miriam Bredow; 1958. New York, Toronto, London: McGraw-Hill Book Company, Inc. 9" × 5¾", pp. 448, with many illustrations. Price not stated.

THIS book was written to provide a training and reference text for lay medical assistants, of whom there is apparently an increasing number in the United States. Indeed, according to the preface, about 75% of all doctors in that country employ one or more aides in their offices. The book contains a fund of useful information about minor medical procedures and the running of a doctor's practice, but conditions of employment in Australia would probably preclude a wide demand for a book of this type.

The Practice of Industrial Medicine. By T. A. Lloyd Davies, M.D. (Lond.), F.R.C.P. (Lond.), with a chapter on "The Hazards of Coal Mining", by J. M. Rogan, M.D. (Edin.), F.R.C.P. (Edin.); second edition; 1957. London: J. and A. Churchill, Limited. 8¼" × 5¼", pp. 292, with 15 illustrations. Price: 30s. (English).

THE author of this book is Professor of Social Medicine and Public Health in the University of Malaya, and so is well qualified for the task that he has set himself. This is to attempt to fill the present serious gap in the education of the medical student and nurse, and to help the practitioner undertaking the work of an industrial medical officer for the first time. The aim has been to fit the separate requirements for industrial health into a composite whole, rather than to study each in detail. After a chapter dealing with industrial medicine in broad terms and a historical and introductory survey, chapters are devoted in turn to medical examination, accidents, fatigue and environment, the social functions of industry, industrial disease and toxicology, the hazards of coal mining, and workmen's compensation and rehabilitation. The concluding chapter is in the nature of an epilogue, simply entitled "The Future". This is a thoughtful and thought-provoking book that should be helpful to anyone undertaking industrial medical practice.

The Anatomy of Judgment: An Investigation into the Processes of Perception and Reasoning. By M. L. Johnson Abercrombie, B.Sc., Ph.D.; 1960. London: Hutchinson & Co. (Publishers) Ltd. 8¼" × 5¼", pp. 156, with illustrations. Price: 37s. 3d.

SOME readers may think at the outset that the earlier part of the book is rather elementary psychology; but they will soon discover that the lightness of touch is deliberate, like the first chapter of a grammar of a foreign language, and they will find themselves, perhaps unexpectedly, in the midst of a serious analysis of their reasoning powers.

All our waking life we are receiving a bombardment of information through our sense organs. Part of this bombardment is ignored; part is selected by reason of its context, and we interpret it in the light of information received in the past. Memories of former experiences and interpretations operate powerfully in the making of our judgements. The factors which are here in action may not enter consciousness as in seeing familiar things; on the other hand, we find that conscious factors operate

as in evaluating evidence from an experiment. We discover on psychological analysis how profoundly the information we select depends on assumption or preconception. All this is presented with a delightful facility of expression, and is illustrated with examples of how easily our judgements may be deflected or indeed rendered fallacious.

The second part of the book contains much original matter, and a detailed account is given of the author's "discussion courses" with medical students, devised to help them in making sounder judgements about scientific matters. The student is encouraged not only to challenge authority, but also to question the validity of his own reasoning. Eight or nine (preferably not more) students are seated in a rough circle, and some word or topic is introduced for explanation or definition. A tape recorder registers the conversation as it actually occurs, giving the broken sentences and verbal repetitions inadmissible in a printed article. For example, the term "normal" led to some animated discussions and interjections of dissent. "Classify' opened out a diversity of opinion quite startling to the students themselves. The two discussions based on these words are given in detail, and their presentation cannot fail to arouse interest and also belief in the method. After a course of such discussions, the student has his confidence in the accuracy of his judgements rather shaken. That this autoanalysis and critical caution will be of value in his professional career is assumed, and we think rightly.

Surgery of Repair as Applied to Hand Injuries. By B. K. Rank, C.M.G., M.S. (Melbourne), F.R.C.S. (England), F.R.A.C.S., and A. R. Wakefield, M.S. (Melbourne), F.R.C.S. (England), F.R.A.C.S., with a foreword by Sir Gordon Gordon-Taylor, K.B.E., C.B., LL.D., Sc.D., F.R.C.S., F.R.C.S. (Ed.), F.R.A.C.S., F.A.C.S., F.R.C.S. (Canada); second edition; 1960. Edinburgh and London: E. & S. Livingstone Limited. 9¾" × 6¾", pp. 298, with 219 illustrations. Price: 45s. (English).

THIS book is now too well known to need a detailed description, and all the praiseworthy features of the first edition are present in the second. It is not uncommon to find textbooks that are first class in their first edition, but become poorer with each subsequent edition. This is often due to the desire to include all sorts of additional material, so that the original spirit and purpose of the work are lost. The authors of this book have not made this mistake with their second edition, and it is a tribute to the original conception of the work that practically no change has been found necessary beyond slight amplification in certain parts and the addition of a small number of illustrations.

In spite of the fashions to which surgery is prone, it is a fact that sound fundamental principles do not alter. The great virtue of this book is that it is entirely based on such principles and deals concisely with their application.

The success of this publication is no longer a matter for speculation. The opinions expressed in the reviews of the first edition, that it would become a standard work on the subject, have been amply fulfilled. Every surgeon who has to deal with injuries of the hand should own this book and be familiar with all it contains.

Surgical Note-Taking: A Booklet for Surgical Dressers and Clerks Commencing Clinical Studies. By C. F. M. Saint, C.B.E., M.D., M.S., F.R.C.S. (England), F.R.A.C.S., and J. H. Louw, Ch.M.; fifth edition; 1960. London: H. K. Lewis & Co. Ltd. 7¼" × 5¾", pp. 180. Price: 12s. 6d. (English).

THIS is the book on surgical note-taking used for over thirty years in at least two leading South African University Medical Schools. In Sydney, where one of the elementary principles of medical teaching is thorough and systematic note-taking, it is remarkable that, whereas medical history-taking is admirably covered in the prescribed text, for surgical history-taking the student is largely dependent on his tutor. The small practical textbook in use is rather concerned with the techniques of eliciting physical signs than with the systematic listing of them.

This book, now in its fifth edition, may supply a long-felt need; it would supplement rather than replace the currently used work, having no illustrations and no details of technique, but giving a series of remarkably complete schemes for examining patients with surgical complaints.

Changes in the new edition consist mainly in the redesigning of chapters, expansion of some and combination of others, but the new edition is not substantially different from the old. A method of gynæcological examination is a welcome inclusion, and the chapters on head injuries and peripheral arterial disease are especially valuable. The pocket dimensions of this book render it suitable for ready reference, and we believe that it would be an asset to any student's library.

The Neurologic Examination: Incorporating the Fundamentals of Neuroanatomy and Neurophysiology. By Russell N. DeJong, M.D.; second edition; 1958. New York: A. Hoeber-Harper Book. 10" × 6¾", pp. 1096, with 368 illustrations. Price: $20.00.

THIS is the second edition of a major work on the neurological examination by the Professor of Neurology and Chairman of the Department of Neurology in the University of Michigan Medical School. The book has not been changed in its general outline from the first edition, but every chapter has been brought up to date with major alterations in some sections to allow insertion of new material. It is divided into ten parts, the first of which deals with the neurological examination in general terms, including the neurological history, the physical examination and the mental examination. The succeeding parts are devoted to the sensory system, the cranial nerves, the motor system, the reflexes, the autonomic nervous system, diagnosis and localization of diseases of the peripheral nerves, nerve roots and spinal cord, diagnosis and localization of intracranial disease, special methods of examination, and the spinal puncture and examination of cerebro-spinal fluid. Based on extensive teaching experience, this book is designed to meet the needs of both undergraduate and graduate students. It is handsomely produced and should be widely acceptable.

Recent Advances in Surgery. Edited by Selwyn Taylor, D.M., M.Ch., F.R.C.S., with a foreword by Sir James Paterson Ross, K.C.V.O., M.S.; fifth edition; 1959. London: J. & A. Churchill Limited. 8" × 5¼", pp. 514, with 160 illustrations. Price: 60s. (English).

THIS is a book already familiar to many surgeons and students. In this fifth edition the principle of multiple authorship has been adopted, and there are now 28 contributors, each of whom is an outstanding authority in his field. Each writer presents his section in a clear and authoritative manner, reviewing the significant changes that have occurred during the past five years, and evaluating the various methods of treatment in current use. In addition, there are many references to the surgical literature; these have been well chosen and will be particularly helpful where more detailed reading is desired.

The range of subjects covered is comprehensive, and includes general topics such as cross-infection, body fluids and the artificial kidney, in addition to the surgery of the gastro-intestinal tract and many of the surgical specialties. Whilst it is obviously impossible to cover every aspect, it is surprising that there is no reference to the surgery of the biliary system or to carcinoma of the colon and rectum.

This is a splendid book, which will be of inestimable value to all concerned with surgery.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Surgery of the Hand", by William L. White, M.D. The Surgical Clinics of North America, Volume 40, Number 2, April, 1960. Philadelphia, London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Limited. 9" × 5¾", pp. 334, with illustrations. Price: Cloth binding, £8 2s. 6d. per annum. Paper binding: £6 15s. per annum.

"Current Therapy—1960: Latest Approved Methods of Treatment for the Practising Physician", edited by Howard F. Conn, M.D.; 1960. Philadelphia, London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Limited. 10¾" × 8", pp. 840. Price: £6.

"Heritable Disorders of Connective Tissue", by Victor A. McKusick, M.D.; Second Edition; 1960. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical) Limited. 10" × 6¾", pp. 334, with many illustrations. Price: £6 12s.

"Communicable and Infectious Diseases: Diagnosis Prevention Treatment", by Franklin H. Top, A.B., M.D., M.P.H., F.A.C.P., F.A.A.P., F.A.P.H.A., and collaborators; 1960. St. Louis: The C. V. Mosby Company. Melbourne: W Ramsay (Surgical) Limited. 9¾" × 6¾", pp. 812, with 137 illustrations. Price: £11.

The Medical Journal of Australia

SATURDAY, AUGUST 20, 1960.

"MYRIAD-MINDED SHAKESPEARE."

LITERARY CRITICS can no doubt be classified in many ways, but one way is to group them into, first, those who are primarily interested in literary methods, textual variations and so on, and, second, those who are primarily interested in subject matter. Naturally there is a good deal of overlap in most cases. In their leisure hours medical men and women with a taste for literature sometimes join the second group, and less commonly the first group. As a result, every year a small crop of papers on the medical aspects of this writer or that appears in medical journals, and occasionally someone produces a book on a subject of this kind. Whether such writings manage to break into the literary world proper at all frequently, we do not know, but it is probably at most a rare occurrence. The most sympathetic and interested audience may be expected to reside amongst medical colleagues with similar tastes, and very often what is written is intended for "within the family", but a wider appreciation is sometimes to be desired. Papers on the medical aspects of literature appear from time to time in medical journals which would grace any literary journal and which warrant the attention of the literary critic proper, who for all his learning in other ways may fail in his understanding of certain matters through lack of technical knowledge.

These thoughts are evoked by a recent contribution to the field of medical literary criticism, a book on "Shakespeare and Medicine" by a surgeon, R. R. Simpson.[1] This is the first major work on the subject for just a century. It is notable not only for the exhaustive listing, classification and examination of the many Shakespearean passages with a medical flavour, but also for the bold way in which the author enters the lists against the literary scholars on controversial matters despite his humble description of himself as "a non-literary medical". In his discussion of the question of Shakespeare's state of mind when he wrote *Timon of Athens*, Simpson becomes frankly caustic in a way that will amuse and win the approval of most of his medical colleagues. The view of many critics on this question has been that Shakespeare had periods of mental imbalance, and that *Timon of Athens* was written during a phase of mental depression. Certainly it is a depressing play, though not half so terrible or moving as many of the greater tragedies. But Simpson is satisfied after long study of the question that Shakespeare wrote *Timon* in accordance with the fashion and conditions of his own time, and he calls the testimony of psychiatrists to support the assertion that it contains no medical evidence of mental imbalance. He rather implies that the literary critics are out of their depth on this matter. He quotes, for example, the following statement by a literary critic, J. Dover Wilson:

> Look at Shakespeare's dramatic work from 1601 to 1608 as a whole, and the conclusion is, I think, irresistible that, for whatever cause, Shakespeare was subject at this time to a dominant mood of gloom and dejection, which on one occasion at least brought him to the verge of madness.

This he dismisses with a biting comment:

> To the medical mind this is as irritating as the mother who proudly tells a doctor that her dear little boy had "just escaped pneumonia"; and again, to the medical mind, these "irresistible conclusions', like the desire to scratch an itchy spot in public, must be resisted.

Two other medical problems interestingly discussed are the death of Hamlet's father and Lady Macbeth's "turn". It will be rembered that Hamlet's father, according to his own ghost, was murdered by his brother Claudius, who poured poison ("juice of cursed hebenon") into his ear. Questions that have been raised about this include whether it could be done and what poison was used. Simpson gives reasons why he thinks that it was practicable and puts forward the claims of henbane (hyoscyamus) as the poison. If the poison worked in the way indicated, the murder would seem to be, as Simpson suggests, the almost perfect crime. The other problem relates to Lady Macbeth's "turn", which occurs when Macbeth is explaining to Banquo and the others why he killed King Duncan's attendants. Lady Macbeth suddenly cries: "Help me hence, ho!" Macduff is solicitous and says (presumably to servants): "Look to the lady." However, none seems to take much notice, and after further conversation Banquo repeats the order: "Look to the lady." Whereupon, the stage directions state, Lady Macbeth is carried out. The question is whether or not Lady Macbeth fainted. Simpson considers the matter at some length and points out, convincingly enough, that she was just not that sort. We may well agree with his pithy summing up that "Lady Macbeth's 'faint' was a feint".

Simpson lists 712 medical references in Shakespeare's writings, 450 being of a major medical character. This is possibly, as he says, a conservative estimate, but more important than the number is the quality of the references. Especially in the chapter on Shakespeare's clinical descriptions, an abundance of examples is produced to show the acuteness of the poet's powers of observation and his remarkable insight into human ills and suffering. Particularly notable are the death of Falstaff in *Henry V* and the terrible description of the effects of tertiary syphilis in *Timon of Athens*, as it was hurled at Alcibiades' mistresses by Timon, but there are many others. In the medical field alone there is ample vindication of Browning's estimate of Shakespeare: ". . . whose insight makes all others dim." Commenting on Shakespeare's knowledge of medicine, Simpson states that it corresponded closely to that prevailing at his time among its professors. This puts it by modern standards at an exceedingly low level, but the fact must be said to add lustre to rather than to diminish the brilliance of his clinical descriptions. Where his medical knowledge came from is not clear. There is good evidence that he held in high regard the

[1] "Shakespeare and Medicine", by R. R. Simpson, M.B., Ch.B., F.R.C.S., F.R.C.S.Ed., 1959. Edinburgh and London: E. & S. Livingstone, Limited. 8¼" × 5¼", pp. 170. Price: 25s. (English).

best physicians of his day, and Simpson points out that he never portrays a bad doctor among the considerable number of medical characters in his plays. One of the most interesting chapters in this book is that devoted to John Hall, physician, who was Shakespeare's son-in-law, and appears to have been a man of sincerity and integrity in both his personal life and his medical practice. Shakespeare may well have been influenced by the character and qualities of Hall in the portrayal of doctors as doctors in the plays, as Simpson suggests, but apparently there is no evidence to indicate that Hall influenced the medical references in the plays, either in their quality or in their quantity. "There is, indeed", Simpson writes, "no necessity to assume that Shakespeare's medical references, with all their strikingly apt and amazingly rich medical imagery, were any more influenced by a doctor than there is to make a comparable assumption about his references to naval and military matters, to music and the law, and the many others. They were all the products of the mind of this genius, Shakespeare. And who shall set bounds or limits to the genius of Shakespeare's mind?" In medicine, as in other things, the greatest English poet, perhaps the world's greatest poet, justifies Samuel Taylor Coleridge's phrase, "our myriad-minded Shakespeare". Coleridge states that he borrowed the phrase from a Greek monk, who applies it to a Patriarch of Constantinople, but its transfer to the poet is most fitting, and Coleridge's justification for this is wholly to be approved: "It seems to belong to Shakespeare, *de jure singulari, et ex privilegio naturae.*"

Current Comment.

THE PROGNOSIS IN NEPHROBLASTOMA.

NEPHROBLASTOMA or Wilms' tumour is a subject which for many reasons has long attracted considerable attention, but it is nevertheless rare, and the evaluation of its prognosis and the results of different methods of treatment are befogged by the absence of any really large series. There is general agreement that the prognosis has improved over the past three decades, but there are still remarkable differences among the results of recently published series from Britain and America; nor is there any real agreement as to the most important causes of the improved prognosis. Three years ago Russell Howard[1] reported a series of 26 cases seen at the Royal Children's Hospital, Melbourne, in which there were only three survivors; this series included patients who were regarded as inoperable when first seen. In 1956, L. S. Scott[2] presented an analysis of 63 cases seen at the Royal Hospital for Sick Children, Glasgow, and compared them with over 1500 cases abstracted from the medical literature. There were only six survivals in the Glasgow series, but most of these were among the more recently treated patients. Among the published cases, the survival rate among 458 cases seen before 1935 was 8·5%, among 411 cases seen between 1935 and 1944, 18%, and among 712 cases seen between 1945 and 1954, 22%. However, two recent American reports paint a very much more optimistic picture. R. S. Owings and M. Radakovich report on 18 patients with Wilms' tumour treated at Rochester in the past 30 years, 10 of whom have survived. (Their criterion of survival is based on a "period of risk" calculated from the age of the child when the tumour is discovered *plus* nine months; i.e., if the diagnosis is made when the child is two years old, the "period of risk" is 33 months—if the child is well 33 months after removal of the tumour, a cure is claimed.) An important point is that of their nine patients aged more than 18 months when the tumour was diagnosed, only one survived, but of nine who were under 18 months when the diagnosis was made, all survived. The much better prognosis in very young children is emphasized in all recent reports. J. K. Lattimer, M. M. Melicow and A. C. Uson have published two reports[4,5] on a series of 42 children with Wilms' tumours treated since 1934 at the Columbia-Presbyterian Center, New York. Sixteen of their patients have survived for two years or longer, a survival rate of 38%. However, if their figures are broken down according to age groups, it is seen that eight out of the nine children whose condition was diagnosed before the age of one year survived, while three of the six between one and two years of age survived, and only five of the 27 over two years of age did so. One of the patients in this series had his tumour removed when only four days old, and was alive and well two years later. Another point of prognostic importance is the exact site of the tumours, those arising in the lower pole of the kidney having a very much better prognosis than upper pole tumours; this can be explained on purely anatomical grounds. Lattimer *et alii* employ two years as their minimum survival period in claiming cures, on the grounds that of the 20 patients in their series who have died, 17 did so in the first two years after treatment, one died in the third year, one in the fourth, and in one who died 10 years later as a result of hydronephrosis of the opposite kidney, no tumour remnants could be found at autopsy. In some other series 18 months' survival has been taken as evidence of cure, but this has been criticized.

Radiotherapy has sometimes been given much of the credit for the improved survival figures, but other factors are possibly more important. In earlier years, when the long-term survival rate was less than 10%, the operative mortality was high, and there may have been some reluctance to hasten to such a formidable operation in young children. However, recent series show a great improvement in this respect, and there were no operative deaths in either of the two American series quoted. This improved operative prognosis has encouraged what is perhaps the most important single factor, namely, earlier diagnosis and prompt surgical removal of the tumour. At a time when the results of all treatment were bad, strong claims were advanced in favour of radiotherapy, some authors urging the claims of radiotherapy alone. However, as pointed out by Scott,[2] opinion has now swung away from placing too much reliance on radiotherapy, and both the American teams mentioned urge that it should be used with caution because of the severe damage which may result to the spine, leading to serious skeletal deformity in later years. With improved prognosis, this aspect becomes increasingly important. At one stage pre-operative irradiation was widely advocated, but in the most recent reports this is condemned on the grounds that there is no evidence that it improves the survival rate, that it involves delay in operating, and that there is the risk of irradiating benign tumours (e.g. cystic kidneys) without any possible benefit to the patient but with the distinct possibility of doing serious harm. Most authors appear to advocate immediate nephrectomy followed by post-operative irradiation. However, for reasons already stated, Owings and Radakovich seriously question the validity of the routine use of irradiation of the renal fossa in very young patients. Six out of the 10 survivors in their series had bony deformities as a result of this, and they point out that recurrence in the renal fossa is rare, even when numerous metastases are present in the lung; further, they state that in very young children nephrectomy alone in some hands has had very good results. In the series of Lattimer *et alii*, four out of five of their youngest patients, who were treated by nephrectomy alone, survived, and two other reports are quoted as showing equally favourable results in this group. However, these facts should not be construed as an attempt to minimize the importance of irradiation in many cases. Lattimer *et alii* mention one case in which a

[1] MED. J. AUST., 1957, 1: 200 (February 16).
[2] *Brit. med. J.*, 1956, 1: 200 (January 28).
[3] *Surgery*, 1959, 46: 864 (November).
[4] *J. Amer. med. Ass.*, 1959, 171: 2163 (December 19).
[5] *N.Y. St. J. Med.*, 1959, 59: 415 (February 1).

single metastasis appeared in a lung six months after nephrectomy and disappeared after further radiotherapy; six years later the patient was alive and well. In view of the frequency with which metastases appear in the lungs, prophylactic irradiation of the lung fields has been suggested, but not, apparently, widely adopted. Again, as Scott points out, pre-operative irradiation of very large tumours may make their surgical removal technically less difficult.

WHO ASSISTANCE FOR THE CONGO.

THE value of having an international health body such as the World Health Organization has been well brought out by recent events in the Congo, as indeed has been the value on a higher level of the United Nations Organization. On July 22, 1960, the Director-General of WHO, Dr. M. G. Candau, announced that the services of a group of staff members from WHO Headquarters in Geneva were being made available to the Government of the Congo to assist in the organization of the emergency health services. The Assistant Director-General of WHO, Dr. P. M. Kaul, had left on July 21 to act as personal representative of the Director-General, appraise the situation and advise him on any further steps WHO could take to help the Congo. At that stage 16 people from the African Regional Office or from the Headquarters of WHO, representing nine nationalities, were already in the Congo or would be there within a few days to assist the Minister of Health in his task. Most of them were senior officers of WHO, who specialized in such fields as public health administration, sanitary engineering, malariology, laboratory work, nursing, and so on. It was pointed out that the action of the Director-General of WHO was being carried out in close cooperation with the Secretary-General of the United Nations and was in line with the policy adopted by the United Nations in connexion with events in the Congo.

A further announcement by the Director-General on July 26 stated that five senior members of the WHO staff had departed that day for Leopoldville to aid the Minister of Health of the Congo, Mr. Grégoire Kamanga, in the organization of the country's health services. Another WHO staff member, Dr. Athamas Bellerive, had been named Chief Adviser to the Congo's Minister of Health. This brings up to 24 the number of medical, nursing, laboratory and sanitary engineering personnel from WHO Headquarters and its regional offices that have been flown at short notice from various parts of the world to help fill emergency gaps in the Congo's health services.

VIRUS VIRULENCE AND PATHOGENICITY.

THE influenza pandemic of 1918 was, apart from the classical bubonic plagues, the greatest pestilence that has afflicted mankind. During and after the second World War, virologists were fearful of a repetition of the 1918 pandemic, but it did not occur. Then in 1957 a new form of influenza virus, originating in China, spread all over the world. The infection rate with "Asian 'flu" was no less than with the pandemic influence of 1918, but the associated mortality was of a different order. Did this difference depend upon differences in the virulence of the causative viruses of the two pandemics, or upon the successful drug treatment of associated bacterial infections in 1957?

This was one of the questions debated last year by a group of virologists assembled by the CIBA Foundation as a Study Group on "Virus Virulence and Pathogenicity". The Study Group was under the chairmanship of Sir Macfarlane Burnet, and was held in honour of Professor J. Mulder of Leiden, who has made a special study of human influenza over the last thirty years. The contributions to the Study Group have now been published in a volume which includes short papers on different aspects of virus virulence by Professor C. H. Stuart-Harris, Professor H. R. Morgan and Professor J. Mulder, and by Dr. C. H. Andrewes, Dr. E. D. Kilbourne and Dr. D. A. J. Tyrrell.[1] Each paper is followed by a summary of the subsequent discussion, from which many interesting points emerge. Attention was concentrated on influenza and, to a lesser extent, on poliomyelitis. It is pleasing for Australians to note the use made of local observations on changes in the virulence of myxoma virus.

The book contains an interesting discussion on topics of considerable importance to public health workers, and sets out the current views of leading virologists on the epidemiological importance of variations in virus virulence.

Ignorance of the nature of the virus responsible for the 1918 pandemic makes final judgement of the relative roles of virus and bacterial invader impossible. Dr. Kilbourne argued a minority view in saying that influenza virus had not varied in its virulence for man over the last seventy years; the consensus of opinion was that there were changes in virulence as well as in the severity of the associated bacterial infections.

SERVICE IN MEDICINE.

PESSIMISTIC PEOPLE who feel that the younger generation of our profession is unduly preoccupied with financial gain may have their spirits lightened a little by the following paragraph taken from the Monthly Bulletin, July, 1960, of the Western Australian Branch of the British Medical Association:

> Custom forbids us to write his name with pride, but we would like to. It was recently necessary to send an "iron lung" to the Kimberleys for two children suffering from severe poliomyelitis. No one with the necessary experience was available from I.D.B. or elsewhere in the Public Health sphere. A young G.P. who had had experience with the iron lung was approached, and he left his practice in the hands of a partner, left his family and flew to Derby, where he remained for four or five days. He cared for the sick children in the north and then supervised their removal to Perth. The Health Department asked for this practitioner's account and he said that he did not propose to charge any fee for his services.

THE HAPPY COLLEGE STUDENT MYTH.

M. L. SELZER is one of three psychiatrists who work at the Mental Hygiene Clinic of the University of Michigan, which is an integral part of the University Health Service. In a recent article,[1] he states that each year some 8% of the student population attend this clinic and that approximately 40% of these are self-referred. Of 506 students interviewed, 35% were neurotic, 24% had personality disorders and 21% were schizophrenic. Selzer points out that these findings are in contrast to previous published reports which leave the impression that university students' emotional disorders are largely transient, with a substantial number suffering no worse than mild adjustment reactions. He suggests that at university clinics many patients are "under-diagnosed", and comments on some of the reasons for this. Among these is the "myth" fostered by journalists and the students themselves that they are having a wonderful time, with everyone relaxed and well adjusted. He states that there is reason to believe that patients seen by a college health service psychiatrist are diagnostically comparable with patients encountered in any out-patient psychiatric clinic accessible to the public.

[1] "Virus Virulence and Pathogenicity", in honour of Prof. J. Mulder, edited by G. E. W. Wolstenholme, O.B.E., M.A., M.B., M.R.C.P., and Cecilia M. O'Connor, B.Sc.; Ciba Foundation Study Group No. 4; 1960. London: J. & A. Churchill Limited. 7¼" × 4¾", pp. 128, with illustrations. Price: 12s. 6d. (English).

[1] *A.M.A. Arch. gen. Psychiat.*, 1960, 2:131 (February).

Abstracts from Medical Literature.

GERIATRICS.

Unexplained Heart Failure in the Aged.

G. A. ROSE AND R. R. WILSON (*Brit. Heart J.*, October, 1959) discuss a retrospective study of 50 consecutive necropsies on patients who died at an age of 70 years or over with heart failure for which no adequate cause had been found during life. The findings have been compared with those of a group of 50 patients matched for age and sex in whom, prior to death, no heart disease had been suspected. Auricular fibrillation was common in both groups and did not appear to be related to coronary artery disease. It was associated with dilatation of the heart. Of 18 men and 32 women with unexplained heart failure, three men and 15 women had no valvular disease, right ventricular hypertrophy, significant pulmonary disease, significant hypertension or notable cardiac hypertrophy. It is postulated that they may represent an entity of "senile heart failure". Brown atrophy was found in 20% of heart-failure subjects and in 36% of the control series.

Senile Cardiac Amyloidosis.

J. S. GOLDEN *et alii* (*Amer. Heart J.*, March, 1960) discuss at a clinico-pathological conference the case of a man of 84 years who died after a prolonged illness, manifested by congestive heart failure and hypertension, which required repeated admissions to hospital over a three year period. Sudden death followed institution of quinidine therapy. Post-mortem examination showed advanced severe occlusive coronary artery disease. In addition there was focal and massive replacement of heart muscle with amyloid. Amyloid was also found in the blood vessels in other organs. Current theories as to the cause of this condition are discussed and include among others, malnutrition, senility and degeneration of elastic fibres; none are really satisfactory.

L. BUERGER AND H. BRAUNSTEIN (*Amer. J. Med.*, March, 1960) draw attention to the relative frequency of this condition. They describe a survey of the autopsy material at the Cincinnati General Hospital covering two periods of several years and a large number of cases. The hearts of all patients over 55 years of age who had come to autopsy were examined for hyaline areas in the heart sections; when they were discovered, they were checked for amyloid by staining with crystal violet. Of the 1325 cases studied between 1953 and 1956, 2·3% had definite amyloid deposits. These tended to be interstitial, beneath the endocardium and epicardium and in the heart valves. There was an increase in the incidence with advancing age, and eight of the 33 patients over 90 years had the condition. There was no evidence that the severity of the condition increased with age, and there was no evidence of resorption of the deposits. The authors suggest that the condition makes its appearance over one or two years and thereafter remains stationary. The heart weight was not increased in the affected subjects, and race and sex appeared to have no influence. The amyloid deposits in the 42 affected subjects were restricted to the heart and blood vessels, especially the blood vessels of the lung and pancreas. The authors conclude by stating that the condition should be suspected in the presence of congestive heart failure unexplainable by other causes. They note that heart failure occurred only in those with extensive deposition of amyloid.

HYGIENE.

Epidemiology of Dog Bites.

H. M. PARRISH *et alii* (*Publ. Hlth Rep.* (*Wash.*), October, 1959) have made an epidemiological survey of dog bites to elicit various human, dog, and environmental factors associated with them that would indicate ways of prevention and control. During July and August, 1958, 947 dog bites occurred in Pittsburgh, U.S.A. The incidence of bites per 10,000 human population was 19·46 for males and 8·84 for females; 76% of the victims were less than 20 years of age. High risk groups identified were: school children, pre-school children, persons coming to the dog owner's house in the course of work, such as newspaper boys, postmen and veterinary surgeons. The distribution of bites was as follows: 76% were inflicted on the extremities, 16% on the head, face and neck, and 8% on the trunk. Only about 10% of the bites were moderately severe or severe. None of the bites was fatal. A high percentage of facial wounds required subsequent plastic surgery. About one-third of the bite accidents resulted from dogs biting maliciously without human provocation, one-third happened while the victims were petting or playing with dogs, and one-third were attributed to human activities which caused the dogs to bite. The following environmental factors were identified: 65% of the bites were inflicted near the dog owner's home; most bites happened during the spring and summer months; and 79% of the bite accidents occurred between noon and midnight. The authors make suggestions about what to avoid in dealing with dogs, to guard against the risk of being bitten.

Accidental Poisoning in Young Children.

I. H. RUSSELL, S. MACKENZIE AND G. MCPHAIL (*Med. Off.*, April 29, 1960) carried out a series of experiments to ascertain the efficacy of two medicine bottles with special safety caps and four locking devices for cupboard doors. One hundred and nine children from 14 months to five and a half years of age were given the problem of getting sweets out of the bottles and containers. The first bottle was opened by 59% of the children in from five seconds to 4·5 minutes. The second was opened by 12% in from 90 seconds to five minutes. The cupboard with a knob and spring catch was opened by 67% of children; the cupboard with a knob and sliding bolt was opened by 28%; the cupboard with lock and key and no knob was opened by 45%; and the cupboard with a safety catch that had to be moved before the handle would open the door was opened by 15%. The authors commented on the pertinacity of the children in their efforts to "get at" something interesting in the containers and the danger of relying on locking devices to keep poisons away from children.

Staphylococcal Food Poisoning.

B. E. HODGE (*Publ. Hlth Rep.* (*Wash.*), April, 1960) surveyed 95 outbreaks of staphylococcal food poisoning. The organisms, the types of food, infected food handlers, unclean practices during food preparation and treatment given to the food after preparation were factors investigated in each outbreak. In conclusion the author considers that the determining factor in the development of staphylococcal food poisoning is the keeping of cooked protein food warm or at room temperature for four hours or longer. Of 83 fully reported outbreaks, the vehicles in 95% were cooked protein foods which were subsequently kept unrefrigerated or warmed. Outbreaks commonly occur when the food is handled cleanly by personnel who are free of infections. The widespread presence of pathogenic staphylococci among healthy persons insures widespread contamination of food regardless of care in handling. To prevent staphylococci in cooked protein food from forming enterotoxin the author recommends 40° F. as the maximum temperature for keeping cold, cooked protein food, 140° F. as the minimum temperature for keeping hot, cooked protein food, and three hours as the maximum length of time for which cooked protein food should be kept between 40° and 140° F.

Study of the Effects of Air Pollutants on the Eye.

S. R. METTIER *et alii* (*A.M.A. Arch. industr. Hlth*, January, 1960) have studied the effects of noxious gases in concentrations found in "smogs". Rabbits were exposed to acrolein (2 p.p.m.), ozone (2 p.p.m.), sulphur dioxide (20 p.p.m.) and nitrogen dioxide (20 p.p.m.), acutely and chronically. Under these conditions no ophthalmological or biochemical effects were noted on intact or on deepithelialized corneas. This suggests to the authors that the sensory mechanism of the eye is more sensitive to these gases than are the more fundamental metabolic processes such as enzyme activity, energy production and cellular growth, and provided the concentrations of these gases in "smog" do not exceed those used in this study no damage will result to the eye from exposure to "smog".

Poliomyelitis Immunization Publicity.

W. A. ALLEN (*Publ. Hlth Rep.* (*Wash.*), March, 1960) outlines methods used to motivate residents in Philadelphia to become immunized against poliomyelitis. After an increased incidence of poliomyelitis in 1958, a special immunization programme was instituted in areas where response to previous attempts to increase

the number of immunized people had been poor. The response was poor and the area was faced with a possible poliomyelitis epidemic. A special house-to-house immunization campaign was then undertaken, with mobile immunization teams which consisted of a physician to give injections, a public health nurse to go from door to door to tell residents about the injections, a graduate nurse to assist with the injections, a health educator to organize local voluntary assistance, a clerk to record injections, and a sanitarian to drive the vehicle and make announcements over the loud speaker. The results revealed that this type of direct approach, particularly to groups which do not respond to the usual approaches, can be of great value in increasing participation in immunization programmes. Of the people responding to the campaign, the majority were in the age groups most susceptible to poliomyelitis, in which the immunization level was particularly low.

Enteropathogenic Escherichia coli from Household Pets.

K. A. MIAN (*J. Amer. med. Ass.*, December 5, 1959), commenting that there is an accumulation of good evidence which points to *Escherichia coli* as the cause of infantile diarrhœa, reports the results of a bacteriological investigation of enteropathogenic *E. coli* in household pets over a period of one year. Specific serotypes and biotypes of enteropathogenic *E. coli* $0111:B_4$, $055:B_5$, $026:B_6$, $0127:B_8$ and $0125:B_{15}$ were isolated from 237 dogs and 84 cats, of which 12·5% were found to be carriers of serotypes. The incidence was higher during the summer months, when outbreaks of diarrhœa in humans are most common. During the course of the investigation an 11-month-old baby was brought to hospital with gastro-enteritis due to *E. coli*. The identical strain was recovered from a dog in the same household, while examination of stools from the patient's father, mother and sibling all gave negative results.

Accident Mortality Data as Epidemiological Indicators.

A. P. ISKRANT (*Amer. J. publ. Hlth*, February, 1960) has applied the epidemiological approach to the study of accidents. Available data in U.S.A. regarding host, agent, environment and their interaction are considered under a number of headings. Accidents are a leading cause of death in every age group from one to 35 years, and in the 15 to 24 years age group cause more deaths than all other causes combined. Host factors investigated were age, sex, race, marital status, and physical conditions. The lowest accident death rate in the United States is in the school-age group. Drowning and bicycle accidents are important causes of death in this group. Accidental death rates are highest at the two extremes of life when individuals are least agile. Motor-cars are the most important factor in accidents in the 15 to 20 years age group, and deaths from motor-car accidents in this group are increasing. Males have a higher death rate from accidents than females, except in the 85 and over age group, where deaths from accidental falls are more frequent in females. In general, accidental death rates are higher for non-white than for white persons, and there are fewer accidental deaths among married than unmarried people. In regard to the agent, the motor vehicle is the one most commonly involved, 40% of accidental deaths being associated with motor vehicles. Falls are the next most common cause. About two-thirds of fatal falls occur at home, most frequently in the bedroom. Fire and explosion, drowning, and poisoning come next in that order. Environmental factors such as geography, season, time of day, weather and location may be of importance. For example, deaths from motor-car accidents are relatively higher in mountainous areas and deaths from drowning are highest in the summertime. The author considers that similar investigations into conditions associated with accidents would assist in discovering effective measures of prevention.

Prophylaxis for Otitis Media.

P. R. ENSIGN, E. M. URBANICH AND M. MORAN (*Amer. J. publ. Hlth*, February, 1960) report the result of an attempt to prevent otitis media by mass medication. A group of 124 children all less than 11 years of age were given sufficient sulphamethoxypyridazine three times a week to maintain blood sulphonamide levels of 5 to 15 mg. per 100 ml. None of the study group who took the medication regularly had earaches or draining ears, but 12·6% of the control group without previous draining ears had otitis media during the year. This regimen was shown to be successful in preventing otitis media in children who had had draining ears, provided the drums had healed. In children whose drums had been destroyed or badly mutilated it is less successful, but has proved valuable in a small number of cases in suppressing discharge.

THERAPEUTICS.

Tolbutamide in Paralysis Agitans.

E. W. GATES AND I. HYMAN (*J. Amer. med. Ass.*, March 26, 1960) state that they noticed a marked diminution in tremor of the hands and fingers of a diabetic patient, who also suffered from Parkinsonism, after he began treatment with tolbutamide. They then began to use tolbutamide for other patients with paralysis agitans, and report their findings in 15 patients so treated. All suffered from paralysis agitans of long standing, and 11 of these showed a considerable decrease in rigidity or tremor, or both. Several showed marked improvement in the mask-like facies with return of a more normal smile. In several, improvement of speech was noted. It is stated that improvement was not related to hypoglycæmia, and that the mechanism of the action of the drug is not understood. Care was taken to eliminate the psychological effect of treatment with a new drug. The dosage employed was one gramme two or three times daily, and the authors recommend that all patients who are given tolbutamide for paralysis agitans should take light snacks or sweetened drink between meals. They state that their results were consistent and indicate the need for further research on man or animals.

Idiopathic Thrombocytopenic Purpura.

A. F. CARPENTER *et alii* (*J. Amer. med. Ass.*, December 5, 1959) discuss the treatment of thrombocytopenic purpura. They state that this condition is of unknown ætiology, and used to be treated mainly by splenectomy. However, since steroids have been used for the disease, splenectomy is less often resorted to. In the series of 85 consecutive patients studied, 24 did not have steroids or splenectomy, but 10 of these had complete remissions within a year. All 10 were under 10 years of age and each had had an infection within a month before the onset of purpura. Sixteen other patients had received steroids without splenectomy, 26 had a splenectomy but no steroids, and 19 had steroids and splenectomy. Complete remissions were obtained in 81% of splenectomized patients and only 38% of those treated with steroids. The dose of steroids in most cases was equivalent to 15 to 40 mg. of prednisone daily. The duration of treatment varied from two days to 66 months. The relationship of recovery to steroid therapy was uncertain in several patients, especially those who had suffered infections before the development of purpura. The authors conclude that patients aged less than 11 years, and perhaps those up to 23 years, should be observed for from seven to 12 months before expectation of complete spontaneous remission is abandoned.

The Treatment of Polycythæmia with Radioactive Phosphorus.

L. SZUR, S. M. LEWIS AND A. W. G. GOOLDEN (*Quart. J. Med.*, July, 1959) discuss the treatment of polycythæmia vera with radioactive phosphorus (^{32}P) in a review of 90 cases seen at Hammersmith Hospital. They describe the symptomatology and clinical findings in these cases, and give the hæmatological data, including blood volume measurements. Methods of treatment before the introduction of ^{32}P are briefly reviewed. Thirty-five patients in the authors' series had received previous treatment elsewhere, 20 by venesection, 11 by external irradiation and four by phenylhydrazine. The technique and dosage problems of ^{32}P therapy are discussed, and the results obtained in 78 patients whose progress had been followed for at least one year are presented. Of these patients, 64 had obtained a full remission, which is defined as the disappearance of all reversible symptoms and a return of the blood picture to within normal limits for at least six months. In some patients remissions had lasted up to 80 months. It is noted that in any one patient remissions after treatment tend to be of similar or even identical duration, unlike the response in chronic leukæmia, in which the periods of remission tend to become progressively shorter. The problem of leukæmia and myelosclerosis in relation to polycythæmia vera and to ^{32}P are discussed. Two patients in the present series have so far developed leukæmia, and both of these had previously been treated by external radiation. The authors conclude that at the present time ^{32}P is the treatment of choice in polycythæmia vera.

Clinico-Pathological Conferences.

A CONFERENCE AT SYDNEY HOSPITAL.

A CLINICO-PATHOLOGICAL CONFERENCE was held at Sydney Hospital on October 20, 1959. DR. W. WOLFENDEN was in the chair. The principal speaker was DR. RALPH READER, Honorary Assistant Physician of the Royal Prince Alfred Hospital, Sydney.

Clinical History.

The patient was a man, aged 34 years, a worker in a brass foundry, who had been well until three weeks before his admission to hospital. While at work on Friday, July 3, 1959, he noticed sudden weakness of both legs after he had been sitting. There was no sensory accompaniment; his legs would just not support him. This lasted for a short time before he was able to walk about and resume work. Thereafter he felt generally unwell for the next two days, but returned to work on the following Monday. However, he reported to his doctor on the Monday evening, and was told that his blood pressure was elevated. For the rest of the week he remained in bed, although he felt well, and he was admitted to Bankstown Hospital on July 11 because of the finding of an elevated blood urea level. During the following week he developed anorexia and nausea and had occasional vomiting, and on July 18 he developed pleuritic chest pains across the front and back of his chest. These were accompanied by an unproductive cough and hot and cold shivers. He was given penicillin. Over the next two days the urine volume was noted to be diminishing, sore throat developed and vomiting became more severe. He was then transferred to Sydney Hospital for management of his oliguric renal failure. There was no past history of renal or other diseases.

At Sydney Hospital the findings on examination of the patient were as follows. He appeared ill, pale, dyspnœic and drowsy. His blood pressure was 200/90 mm. of mercury, his pulse rate was 110 per minute and his temperature was 100·6° F. The venous pressure was not elevated. There was no œdema of the legs or back. The heart had dual rhythm and was not enlarged, but there was an apical pleuro-pericardial friction rub. Examination of the chest revealed diminished movement, air entry and vocal resonance at the base of the left lung and crepitations at both lung bases. The mouth was clear, but the fauces were injected and the uvula was swollen and red. In the abdomen, guarding of the right rectus was found. The liver, spleen and kidneys were not palpable. No abnormality was detected in the central nervous system. There was no lymphadenopathy, and the fundi were normal.

Dialysis on the artficial kidney was performed on the day after his admission to hospital because of a serum potassium level of 9 mEq/l. with electrocardiographic changes. The anæmia persisted, the maximum urine output being 100 ml. on only one occasion. Treatment consisted of fluid restriction, a protein-free diet, and dialysis repeated twice at weekly intervals because of anæmia with the blood urea nitrogen level in excess of 200 mg. per 100 ml. The course was complicated by intermittent pyrexia with recurrent pleural and pericardial friction rubs and inconstant basal systolic murmurs. Signs of pulmonary congestion and basal effusions remained throughout. Penicillin by injection and later chloramphenicol and erythromycin were given, and the fever abated. Paroxysms of auricular fibrillation developed after the second dialysis and were controlled by digoxin. The blood pressure remained in the range 140/60 to 120/80 mm. of mercury. A transient hæmorrhagic tendency occurred, with epistaxis and bloody motions. Drowsiness supervened, and death occurred in a syncopal fashion after 27 days of anuria, 44 days after the onset of the illness.

The investigations carried out gave the following results. On July 23, the hæmatocrit was 27·5%, and the leucocytes numbered 21,300 per cubic millimetre and neutrophilia was present. The erythrocyte sedimentation rate was 130 mm. in one hour. An X-ray examination of the chest revealed an effusion on the left side, consolidation at the base of the right lung and cardiac enlargement. The serum sodium content was 130 mEq./l., potassium 7·9 mEq./l., carbon 185 mEq./l. and carbonic acid 17·0 mEq./l. The blood urea nitrogen level was 145 mg. per 100 ml., and the serum calcium, phosphorus and cholesterol contents were respectively 8·6, 14·2 and 190 mg. per 100 ml. The total serum protein content was 7·5 grammes per 100 ml. An electrophoretogram gave the following findings: alpha-1 globulin 47%, alpha-2 globulin 23%, beta globulin 12%, gamma globulin 18%. Culture of the sputum yielded a growth of *Proteus*; no growth was obtained on culture of the blood. On July 31, the blood urea nitrogen content was 184 mg. per 100 ml. The serum sodium, potassium, chloride and carbonic acid contents were respectively 145, 7·4, 96 and 14·5 mEq./l. The serum calcium and phosphorus contents were respectively 7·6 and 28·4 mg. per 100 ml. On August 4, the blood urea nitrogen level was 222 mg. per 100 ml. The serum sodium, potassium, chloride and carbonic acid contents were respectively 148, 5·6, 92 and 16·5 mEq/l. The hæmatocrit was 22%, neutrophilia was present, and platelets were plentiful. On August 6, after dialysis, the blood urea nitrogen level dropped from 258 to 144 mg. per 100 ml. On August 11, renal biopsy was undertaken.

Clinical Discussion.

DR. W. WOLFENDEN: We have the pleasure this afternoon of welcoming Dr. Ralph Reader, of Royal Prince Alfred Hospital. The proceedings today are a little different from previous meetings, in that Dr. Reader has seen the patient during life. Even though he does not know the result of the biopsy or the autopsy result, his association with the patient should make his discussion more interesting.

DR. R. READER: Thank you, Dr. Wolfenden. The opportunity of seeing the patient in life has not made discussion of the problem easier, even though it may make it more interesting.

To review the story: The patient was a young man of slight build and normal appearance, in spite of several dialyses on the artificial kidney, and when I saw him I had the impression that he must have been in normal health before this illness started on July 3. The onset was peculiar and dramatic; while at lunch in his place of employment, a brass foundry, he was quite suddenly unable to walk for a short period. Apart from this transient weakness there were no other neurological phenomena, and he was soon able to resume work. Over the following two days there was no notable change, and he returned to work on the following Monday. He felt unwell and reported to his doctor on that evening. The only information we have from that visit is the patient's statement that high blood pressure was detected. Blood was taken for urea estimation, which subsequently was shown to be 130 mg. per 100 ml., so that within a few days of the onset there was considerable nitrogen retention. By the time the result of the blood urea estimation was available, admission to the suburban hospital was arranged. There is not a great deal of information about the findings there. Hæmaturia was detected, proteinuria was mentioned and blood pressure was 160/110 mm. of mercury.

He was thought to be a fairly straightforward case of acute nephritis, and was being treated along those lines when a change occurred. He developed shivers. About the same time his urine output decreased, and he became oliguric over the next week and was admitted to Sydney Hospital. The findings were not very different at Sydney Hospital. He was anuric and uræmic, his blood pressure was 200/90 mm. of mercury. The respiratory symptoms were still prominent. Fever remained with pleuritic pains, and a pleuro-pericardial friction rub was noted. There was no congestive cardiac failure. He was quite clearly a problem of severe acute renal failure, and there were no definite features at that time to indicate the basis of this renal failure, but it had been regarded throughout as acute nephritis. There are one or two features which were unexplained by such a diagnosis, particularly the respiratory involvement, and also a finding on admission to Sydney Hospital of guarding and tenderness on the right side of the abdomen. However, most of the facts seem to fit glomerulonephritis, and it was on that basis that he was treated over the next twenty days, symptomatically as it were, by dialysis on three occasions, the indication being a blood urea of 400 mg. per 100 ml. and a serum potassium varying between 7 and 9 mEq./l. Several other features are also worth noting. Serum phosphate on admission to this hospital approximately eighteen days after onset of the illness was 14 mg. per 100 ml., and subsequently rose to 28 mg. per 100 ml. one week later. Calcium was slightly decreased, and there was moderate acidosis. Electrophoretographic figures show diminished albumin fraction and compensatory rise in alpha-2 globulin, with over-all normal total protein level. No help can be derived from these protein figures. Electrocardiogram was consistent with hyperkalæmia prior to the first dialysis. In spite of checking the advance of the uræmia and restoring, to some extent, the electrolytic disturbance to normality on two or three occasions, anuria persisted, and death finally occurred about 40 days after the onset.

In attempting to establish the diagnosis we must consider the differential diagnosis of a rapidly progressive renal failure. There are not so very many conditions which can cause such a picture. One is acute glomerulonephritis. The main features of this case would be consistent. If this were acute glomerulonephritis, it would fall into the unusual 3% to 4% which run a rapidly fatal course, and the histology would show a severe and probably necrotizing glomerulitis involving all the glomeruli. The onset with hypertension and anæmia would be consistent. The hæmaturia and proteinuria would also be consistent.

A second condition to be considered is an acute deterioration in the patient who is already suffering from chronic nephritis. This, one sees in patients presenting with anuria. Usually the deterioration in the renal function has been precipitated by some disturbance of fluid balance, as may be caused by an attack of diarrhœa or vomiting in a patient who, up to this occurrence, has been well and unknown to be suffering from renal disease. I have seen patients die within a week of the onset of gastro-enteritis who were previously not known to have had renal disease, but in whom autopsy has demonstrated such disease. This presents an important diagnostic problem. On the one hand, the patient may be suffering from acute renal failure due to glomerulonephritis or tubular necrosis, requiring a certain line of therapy which involves, particularly, restricted fluid. On the other hand, it may be the patient is in a state of acute dehydration, superimposed on chronic renal insufficiency, and needs fluids in large quantities urgently. The decision must be made promptly at the bedside, with practically no ancillary aid as to which line of treatment will be adopted. The one single criterion to differentiate prerenal types of uræmia from intrinsic renal disease leading to acute uræmia would be the concentration of the urine. If the uræmia were essentially prerenal, the specific gravity may be expected to be high, whereas if the uræmia is due to tubular necrosis or the anuria of acute glomerulonephritis, one expects an isosthenuria urine, but this does not help if the patient is already in a stage of chronic renal insufficiency. I do not know of any way of solving this problem unless the history indicates fluid loss and dehydration. If this help is not available, I believe the lesser of two evils is to cautiously attempt rehydration. This must have been a problem facing the physicians in managing the present patient at the time of admission. There was, however, no real source of dehydration, and events suggested that it was an acute episode and not chronic nephritis complicated with anuria. The X-ray films available suggest small kidneys, which would be in favour of chronic glomerulonephritis. The clinical evidence of preceding hypertension based on an enlarged heart may also support this, but the series of X-ray films now available do not indicate cardiac hypertrophy. I do not think that this patient had chronic nephritis with a superimposed acute episode of some kind.

The next illness to be considered—also important because of its therapeutic implications—is subacute bacterial endocarditis. This is one of the possible causes of acute diffuse nephritis with rapidly developing renal failure. Other features about this patient suggested this possibility; these included the respiratory episode, which could have been embolic, the fever, which responded to antibiotics, and the changing cardiac murmurs. On the other hand, there was no splenomegaly or finger clubbing, and the over-all progress was perhaps too rapid for subacute bacterial endocarditis. Blood cultures were negative. At the time when I saw this patient, the available evidence did not seem to support this diagnosis.

The next disease which can disorganize renal function in this manner would be one of the so-called collagen diseases of the kidney. These are widely known to damage glomeruli severely, and the interesting thing is that this is frequently associated with pulmonary lesions. This association of a hæmorrhagic type of pneumonia with rapidly progressive renal failure was described in 1919 by Goodpasture, and the syndrome is usually known by this name today. It is an illness which runs its course in a few weeks or up to 12 months. It presents, as a rule, as a debilitating illness with weight loss, night sweats and fever, without localizing signs perhaps for some time. Then a series of hæmoptyses may occur, by which time the patient is ill enough for renal failure to be demonstrated, and changes in the lungs consistent with an hæmorrhagic pneumonia are found. This diagnosis one would take very seriously in this patient. He fulfils many of the criteria. The disease occurs in young men most frequently, and both the progress of his renal disease and the features of the respiratory disease would be consistent with Goodpasture's syndrome.

Another respiratory disease associated with progressive renal failure is Wegener's granulomatosis. I do not know that there is any real difference between the two, although the pathologists describe granulomatous lesions in the paranasal sinuses and in the lungs in the latter condition. I would not attempt here to distinguish between the two. Both diseases occur mostly in young men, and both present primarily as renal and respiratory disease, although any of the other features of polyarteritis nodosa may be present. In this patient there are no other systems involved to suggest polyarteritis nodosa.

The last condition warranting discussion is acute tubular necrosis, which may complicate any state of shock, a mismatched blood transfusion, certain toxins and certain drug sensitivities, none of which ætiological factors were apparent in this patient. I would not expect the picture of acute tubular necrosis to be demonstrated later by Dr. Palmer, and without further discussion I would exclude a primary tubular lesion in favour of a primary glomerular lesion.

Before casting any vote between acute glomerulonephritis and one of the collagen diseases, between which I believe the diagnosis rests, there are one or two other features deserving of explanation. The peculiar onset with weakness of the legs lasting only half an hour or so could have been due to hypertensive encephalopathy, a condition which often ushers in an acute nephritis. I cannot suggest the neuro-anatomical explanation of this symptom, but it probably could be explained on this basis. Secondly, it could have been due to hypokalæmic paralysis apparent only in the legs. This, of course, would presuppose chronic potassium-losing nephritis. I think the evidence for this is so slight that it can be disregarded. Occasionally a fairly extensive and dramatic neurological presentation may characterize the collagen diseases. I would not have expected it to clear up so quickly, and I do not believe that this can be taken to support this diagnosis. The possibility of cerebral emboli, which might occur in subacute bacterial endocarditis, can be considered; but the episode was so transient and vague, with little anatomical localization, that I doubt if we can accept such a possibility.

My last suggestion is asthenia or hysteria; but I think this can be excluded because of the patient's obviously normal personality. Of all these unlikely explanations, the one I would be most ready to accept would be that of a hypertensive episode.

The abdominal guarding I do not regard seriously. The auricular fibrillation occurred relatively late in the case, after dialysis, and probably was due to an electrolyte disturbance and hence of no great relevance.

I find it very difficult to decide whether this was a straightforward acute glomerulonephritis with cardiac failure and respiratory infection, or whether to suggest that this was in fact a Goodpasture's syndrome. I believe it was one or the other.

DR. WOLFENDEN: We must congratulate Dr. Reader on a very good summing up of a case in which there are very many partial clues and not very many full ones. The meeting is now open for discussion.

DR. K. B. NOAD: I do not think much can be added to Dr. Reader's careful and excellent discussion of the problem. Of the conditions he mentioned, I feel that, as so often happens at these meetings, when symptoms of involvement of many systems are presented, the collagen diseases may be represented here. Here we have sudden weakness of the legs, which could be caused by sudden interference with the blood supply, sudden cord compression or an electrolytic disturbance, and Dr. Reader has suggested the interesting possibility of collagen disease as a cause of this symptom. In addition we have hypertension, respiratory symptoms, fever, renal symptoms with failure, leucocytosis with neutrophilia, and very high blood sedimentation rate. I doubt whether acute or chronic nephritis could cause elevation of blood sedimentation rate of this degree. Hence, of the conditions Dr. Reader mentioned, I feel that the collagen group of disorders is the most likely cause.

DR. WOLFENDEN: We notice that the fauces and uvula were swollen and red. I wonder what is the frequency of throat infection prior to acute nephritis.

DR. READER: 50% to 70% of cases have this infection.

PROFESSOR H. K. WARD: I would like to ask Dr. Reader, if this were acute glomerulonephritis, was it severe enough to cause diminution in complement?

DR. READER: I am sure it would have, had the serum been taken within the first week or 10 days.

DR. E. FINCKH: From the pathologist's point of view, thinking of renal biopsies, there are three types of change to be expected, corresponding with the diseases that Dr. Reader has mentioned: firstly, nothing at all or something very slight, which you would expect to find in so-called acute tubular necrosis; secondly, an acute disease, particularly acute glomerulonephritis; thirdly, chronic disease with perhaps a superimposed flare-up, either pyelonephritis without past history or chronic glomerulonephritis. I have no way of choosing other than to follow Dr. Reader's reasoning. I would feel that probably the disease is an acute one, on clinical grounds. If it is an acute disease, it will probably be an acute necrotizing glomerulonephritis, of one or other type. Now histologically it may be possible to pick between them—between the diffuse form of acute glomerulonephritis, or the rather more discrete forms seen in systemic lupus or the changes in subacute bacterial endocarditis, or the appearances we have seen in patients with Wegener's granulomatosis, which are rather like those seen in lupus. Histologically it is possible to have a good stab at distinguishing between these if a good biopsy is obtained. There are slight but important differences, but in general they show very much the same sort of change. There appears to be a pattern of reaction to possibly different ætiological agents which lead to a fairly common sort of eventual finding. In acute diffuse glomerulonephritis, the changes are usually pretty diffuse, affecting nearly all glomeruli. The same thing applies to the glomerulonephritis in subacute bacterial endocarditis, which is distinct from the so-called focal embolic nephritis when the lesion is much more localized and usually does not result in the severe disability that we have here. Now I should think that histologically we might expect either very diffuse changes with necrosis and cell proliferation in glomeruli, or else slightly less diffuse changes perhaps affecting individual tufts, which would incline me to the view that it is disseminated lupus.

I should like to ask Dr. Reader a question. I have always thought that Goodpasture's syndrome was a form of nephritis associated with hæmoptysis, that the hæmorrhage was essential to the diagnosis, and in the absence of hæmoptysis there was merely "nephritis with pulmonary changes". What are his views on this ?

DR. READER: I think this boy did cough up blood at one stage. The usual history of Goodpasture's syndrome is intermittent hæmoptysis over many months, and I suppose some months could pass without hæmoptysis occurring. I do not see why the disease could not run its whole course without hæmoptysis. In any case this patient did cough blood.

DR. R. J. ELVY: We are fortunate here in seeing frequently the blood changes in acute oliguric renal failure. We observe a constantly recurring pattern. In the peripheral blood we find a rapid fall in hæmatocrit to perhaps 20 or 25, very early in the illness, perhaps within 10 days. The peripheral blood film shows different abnormalities, including macrocytes, occasional spherocytic cells and some anisocytosis, without much abnormality in the shape of the red cells. Polychromasia is not usually present and they usually do not have a rise in reticulocytes. The erythrocyte sedimentation rate is always very high, with marked rouleaux formation, and an erythrocyte sedimentation rate over 100 is not uncommon. In the white cell series there is usually a neutrophilia, which I gather is due to a change in osmotic pressure, and Dr. Whyte can tell us more about that, and often hypersegmented forms. There is also a lymphocytopenia, which appears by about the tenth day, and which returns to normal after the diuretic phase. The neutrophilia returns to normal at a slightly slower rate, and platelets have always been plentiful.

This patient also had a transient hæmorrhagic tendency. Prothrombin times were within normal range. I gather that the major defect in the clotting mechanism in these patients is an abnormality in platelets with defective thromboplastin generation due to a deficient platelet factor. Other abnormalities in the early phase of coagulation have also been found.

Most of the work on these clotting abnormalities has, however, been done on patients with chronic "uræmia".

DR. WOLFENDEN: Do you regard this patient's degree of anæmia as being due to some chronic condition upon which an acute episode has been superimposed?

DR. ELVY: No, I do not think so. Acute oliguric renal failure can present with an anæmia of this severity, and all the hæmatological features are consistent here with acute oliguric renal failure.

DR. R. H. VINES: This man does seem a little out of my age range. I noted a number of symptoms and signs suggestive of infection. Hence one must think of acute nephritis or an exacerbation of chronic nephritis. Perhaps the low hæmatocrit fairly early in the development of oliguria is more likely to be related to the second of these two conditions suggested by the presence of infection.

DR. ELVY: What dosages of antibiotics would be given to this patient? And are there any rules about doses of antibiotics given to oliguric patients?

DR. P. CASTALDI: The general tendency is to give half the usual dose of chloramphenicol, on the basis that this is the likely proportion removed by the kidneys, hence 250 mg. six-hourly would be a usual dose. Erythromycin we usually give empirically in the usual dose.

Pathological Findings.

DR. A. A. PALMER: The renal biopsy showed about six glomeruli, all of which were nearly completely sclerotic. There was a little cortical fibrosis and some dilatation of the tubules, with hyaline droplet degeneration of the epithelium in a few. The artery walls were thickened. The remote possibility of amyloid disease was ruled out by appropriate stains.

Abstract of Necropsy Report.

The body was that of a thin man, weight 112 lb., height 5 ft. 4 in.

The lymph nodes at the bifurcation of the trachea were enlarged and dark grey. Sections showed silicosis.

The lungs were similar, each showing some small patches of fibrinous pleurisy and a few small fibrous adhesions. There was patchy anthracosis, and the posterior basal regions were congested and had foci of hæmorrhage. Sections showed mild anthracosilicosis, some bronchiolitis and a small hæmorrhagic infarct.

The heart was enlarged, weighing 15 oz. There was a small pericardial effusion, the surfaces were dull and some adhesions and subpericardial hæmorrhages were present. The left ventricle was hypertrophied. There was moderate coronary atheroma. Sections confirmed the presence of pericarditis, probably uræmic.

The kidneys were of normal size (5 oz. and 6 oz.) and similar. The capsule stripped easily, leaving a smooth surface. The subcapsular surface was paler than normal, with multiple petechial hæmorrhages scattered over it. The cut surface showed a normal pelvis and collecting system. The cortex was a little narrowed and paler than normal. The medulla appeared congested, with a few pale streaks running into it. The sections of the kidneys showed severe subacute to chronic glomerulonephritis. Almost all the glomeruli were affected; many showed adhesions and proliferation of the epithelium of Bowman's capsule. There was fine diffuse cortical fibrosis. Most of the tubules were dilated with, in general, rather atrophic epithelium. Thickening of the walls of arteries and arterioles was only moderate.

Diagnosis.

1. Subacute to chronic glomerulonephritis with oliguric renal failure.
2. Uræmic pericarditis.
3 Mild anthracosilicosis.

Out of the Past.

THE N.S.W. ARMY MEDICAL CORPS AND THE BOER WAR.[1]

[From the *Australasian Medical Gazette*, January 20, 1900.]

IN our issue of November 20th, 1899, we commented on the despatch by New South Wales of a Field Hospital and a half Bearer Company with the necessary transport equipment and eight medical officers. Since then events have transpired at the seat of war, which caused the Imperial Government, through the Right Honourable the Secretary

[1] From the original in the Mitchell Library, Sydney.

of State for the Colonies, to cable a request that the other half-unit of the New South Wales Army Medical Corps with its complete equipment should be sent to the front. The half-unit, under the command of Lieutenant-Colonel Vandeleur Kelly, left in the S.S. "Moravian" on the 7th instant. With him are associated as officers of the Corps, Captains W. L. E. Eames (Newcastle), G. A. Marshall (Sydney), Joseph Marshall (Bega), Lieutenants Newmarsh (North Sydney), G. S. Samuelson (Armidale) and J. A. Dick (Randwick).

In addition to these, a number of the most prominent medical practitioners of the colony volunteered for service, and the offers of Drs. MacCormick, Scot Skirving, Cortis, N. Howse, and Horsfall were accepted and these latter gentlemen left for the seat of war on the 17th instant with honorary commissions. The contingent to the Army Medical Corps, now on its way to the Cape, has attached to it a mounted Bearer Section, so that the colony will be represented by probably the most complete medical unit in South Africa.

New South Wales may well feel proud to be represented by men who have made enormous pecuniary sacrifices in order to serve their country. A company of fourteen trained nurses, under Miss Gould, formerly matron of the Sydney Hospital, left also in the "Moravian" with the Army Medical Corps. We understand that South Australia is also sending six trained nurses.

British Medical Association.

VICTORIAN BRANCH: SECTION OF PREVENTIVE MEDICINE.

A MEETING of the Section or Preventive Medicine of the Victorian Branch of the British Medical Association will be held on September 8, 1960, at 4.30 p.m., in the Medical Society Hall, 426 Albert Street, East Melbourne. Dr. R. J. Farnbach, Senior Health Officer of the State Department of Health, will speak on "Public Health in the United States". All interested are invited to attend.

Medical Societies.

PÆDIATRIC SOCIETY OF VICTORIA.

A MEETING of the Pædiatric Society of Victoria was held on September 2, 1959, at the Royal Children's Hospital, Melbourne.

The Surgery of Chronic Cough.

MR. R. HOWARD discussed the surgery of chronic cough. Chronic cough was defined as a cough which was unaccompanied by acute features. It was pointed out that, although cough was usually due to disease in the lung or bronchial tree, there were other causes (such as those present in the nose and throat), and that these had to be eliminated before the site of the trouble was localized to the lung. Extrapulmonary causes would not be discussed.

Mr. Howard went on to say that the clinical history was extremely important in fixing the duration of symptoms, and such other features as the amount of sputum, exposure to tuberculous infection or liability to fibrocystic disease of the pancreas, the possible presence of a space-occupying lesion present in the chest (dyspnœa) and the indication of any relation to a foreign body. Investigation included tests for tuberculous infection and hydatid disease and all the measures at the disposal of the radiologist. Bronchiectasis was the commonest diagnosis, and by far the commonest type of bronchiectasis was post-infective in origin. In those cases the damage tended to be too extensive for operative measures to be recommended; it was most important to allow the disease to reach a definitive phase before making a final assessment. The unilateral, unilobar form of the disease was that which had given lobectomy its deservedly high reputation, and it was still the most important indication for surgical intervention. When a localized cause was operating—for example, in relation to a foreign body or tuberculous ulceration causing a bronchial stricture—localized bronchiectasis amenable to lobectomy was more likely to be produced.

Mr. Howard then said that cystic disease of the lung, although not very common, was an important cause of chronic cough and a definite indication for operative intervention. Lung cysts were apt to develop tension or suppuration. Most important in the latter regard was intralobar sequestration. Those patients, if operated on early, were susceptible to local resection, but after the onset of suppuration were likely to need lobectomy. Hydatid cyst of the lung was still comparatively common and usually unaccompanied by cysts elsewhere. In that connexion it was most important to realize that the specific immunity reactions (Casoni test, complement fixation test) usually gave negative results in children. Radiographic features were usually diagnostic. The presence of a hydatid cyst in the lung was an urgent indication for its removal. Again early operation was conservative, whereas operation at a later stage (after the onset of rupture and infection) might raise the question of lobectomy. A rare cause of chronic cough was neuroblastoma affecting the pleural cavity and lung. Removal of as much as possible of the malignant mass followed by radiotherapy was indicated, although the results were not good.

Mr. Howard finally showed slides from a case of paraffinoma of the lung. He emphasized that that condition was a great rarity in childhood.

MR. N. MEYERS said that he had reviewed 72 cases of hydatid disease in children which had occurred during the past 20 years. Of those cases, the lung was the only organ involved in 36, and in a further nine the lung was involved as well as another organ. He wondered whether that predilection for pulmonary tissue argued a different pathogenesis in children.

DR. H. WETTENHALL stressed the importance of the persistence of the cough, day in and day out, in bronchiectasis.

Medical Practice.

GENERAL PHARMACEUTICAL BENEFITS.

Statement by the Commonwealth Minister for Health.

THE Commonwealth Minister for Health, Dr. D. A. Cameron, on August 4, 1960, issued the following statement relating to the Pharmaceutical Benefits Scheme.

The new Pharmaceutical Benefits Scheme was introduced in the public interest and it will be amended from time to time in the public interest, but not for any other reason. The Government decided to expand the former scheme because it felt that its scope was too limited to meet present-day needs. One of its weaknesses was that it tended to limit doctors' prescribing. It covered some 50% of the prescriptions normally written by doctors. This meant that while one group of patients received medicine free, another group was required to pay for its medicine in full. The Government was anxious to extend the scope of the scheme, but it did not want to place an avoidably heavy burden on the taxpayer in the process. It therefore adopted the principle it had applied to other aspects of the National Health Scheme. This was that it required the beneficiary to accept a small personal share of the cost. It adopted a new and greatly expanded range of medicines, but it asked that the individual recipient should share the cost to the extent of paying the nominal fee of 5s. for each prescription dispensed. Since many of the prescriptions cost £2, £4 and up to £8 each—some in fact even more—this represented what might reasonably be regarded as very good value. The public, I am happy to say, has freely acknowledged this fact.

The major critics of the scheme appear to be certain members of the medical profession. Their complaint appears to be variously that the scheme is now so wide that it involves them in a great deal more office work, or—and this seems to me to be an odd contradiction in terms—that it is not wide enough. It is said that a great many more drugs and preparations should be included. To the extent that the scheme is now wider, I suppose it may be said that it does involve the individual doctor in more clerical work in writing prescriptions, but prescriptions would still have to be written in some form or other whether they were inside the scheme or outside it. It is true that to use the scheme, doctors must comply with its requirements and must make a carbon copy of each prescription. But that requirement applied to the former scheme, in precisely the same way. There are no new or limiting conditions in the new scheme that did not apply to the old. No drug or

preparation that was in the old scheme has been taken off. The prescriber's book on which the doctors and chemists work has been simplified as far as possible, and further revisions are under discussion at this moment, with a view to saving busy professional men's time.

As to the drugs that are or are not listed, I would say this. Unless the Government places on the list every known drug and patent medicine, and unless it removes every limitation on the quantities of drugs that may be prescribed, there will always be some criticism. That is because this question is actually one of personal opinion.

Because that is the case, and to remove the question from the realm of purely personal opinion, the Government has consistently sought the guidance, with regard to the listing of drugs, of the Pharmaceutical Benefits Advisory Committee. This is not a committee of public servants. It is an independent committee of medical and pharmaceutical experts, free from all pressures, whether political or commercial. The doctors who are members of it were chosen from a panel nominated by the British Medical Association itself. They comprise a majority of four on the committee of seven.

No new drug is added to the list of benefits, or removed from it, except on the advice of this committee. Groups of doctors, individual doctors, drug manufacturers and individual citizens are at liberty to submit requests for the inclusion of a drug. The committee's finding determines whether I, as Minister, recommend to the Government that the drug be included or otherwise, and if it is included, in what quantity it should be made available as a pharmaceutical benefit.

A special meeting of this committee was held recently, and its recommendations are now being implemented. They will be given effect from October 1. This will result in about 100 new items being added to the list of pharmaceutical benefits.

But it should be made plain that the proposed additions will not revolutionize the scheme. It is my opinion that no such revolution is called for. The scheme is so vast in its implications and the medical issues so important to the well-being of the community as a whole, that I believe wisdom dictates that we should hasten slowly, achieving success by steady progression rather than risking error as the result of undue haste.

This I would add. I am by no means convinced that the scheme is basically unsatisfactory. I am, in fact, convinced that it is both generous and effective. The public is infinitely better off with it than it would be without it. It is capable of improvement, no doubt, and it is the Government's wish that it should be improved where improvement is shown to be practicable. To suggest that such a splendid conception should be scrapped because it does not suit one section of the community—or a section of a section—while the public at large stands to gain such material benefit, is quite unthinkable.

Obituary.

WALTER PATON MacCALLUM.

WE are indebted to Dr. Angus Murray for the following appreciation of the late Dr. W. P. MacCallum. This is further to the notice that appeared in the issue of August 6, 1960.

Walter MacCallum carried an aura of distinction with him throughout his life, and it always appeared entirely fitting that he should assume positions of responsibility, and thereby influence the affairs of his fellows in whatever conjugation he found himself. This pattern was set in his school days, when he was an outstanding figure in work, sport and qualities of leadership and a natural selection as senior prefect. The prefects' standards of honour, loyalty and discipline remained with him throughout life, and served as a yardstick by which he measured his fellows. No man set himself higher standards of conduct in public and private life, and few could claim to have so consistently maintained them.

To have enjoyed the friendship of Walter MacCallum was a privilege, for he was far from being a gregarious type, and was never more happy than in his own home. Here, as in other days over a College brew, or under canvas in many parts of the world, he was at his best in a small circle of intimates. He was a rapid and omnivorous reader, covering a wide range of most unlikely subjects, which were reflected in the range of his conversation. He had a lively sense of humour, with a particularly keen appreciation of the incongruous and the ridiculous. His choice of the correct word was always a matter of importance, and nothing gave him more delight than rounding off a discussion with a completely apposite phrase or quotation. He was, however, even more a master of the written word, and produced nothing that was not "excellently well penned".

This ability no doubt contributed to the success, or rather the brilliance, of his staff work during the two World Wars. It is a fact, learnt not from him, that his operation orders for the Battle of Mont St. Quentin in 1918 were taken as a model for the Staff College at Camberley. This operation was cited by Haig as "the most successful single episode on the British front", and the result was heard with incredulity by Rawlinson, who told General Monash that it had altered the whole course of the war. It was a very real heart-break to MacCallum that he was not accepted for combatant duties in the last war; but this undoubtedly was the Medical Service's gain. It was in war that he found his finest hour, and here he more than adequately met the challenge of life. We may say of him, as Wordsworth said of his "Happy Warrior":

> Whose powers shed round him in the common strife
> Or mild concern of ordinary life,
> A constant influence, a peculiar grace;
> But who if he be called upon to face
> Some awful moment to which Heaven has joined
> Great issues, good or bad for human kind,
> Is happy as a lover; and attired
> With sudden brightness, like a man inspired;
> And, through the heat of conflict, keeps the law
> In calmness made, and sees what he foresaw.

JAMES THOMSON PATON.

WE are indebted to Professor H. K. Ward for the following account of the career of the late Dr. J. T. Paton.

James Thomson Paton was the son of Dr. Robert Paton, one time principal medical officer of Sydney. He graduated at the University of Sydney in 1911, and started practice in Blackheath in the Blue Mountains. He enlisted early in the first World War, but his health broke down seriously on the troopship, and this misfortune prevented his service overseas for the remainder of the war. At the end of the war he joined the practice of Sir Neville Howse and Dr. John Howse in Orange, and remained in practice in that town for the rest of his life. In 1938 he was admitted to membership of The Royal Australasian College of Physicians. A steady reader, he kept abreast of the development of modern medicine, no mean task in this day and age and in the midst of a busy practice. Conscientious, unassuming and well-balanced, he gained the confidence and regard of his colleagues and the affection of his patients, who trusted his skill, judgement and wise counsel. He was a fine example of the doctor who is consulted both professionally and in other difficulties, because he is understanding, helpful and trustworthy. Of such is the cream of the profession. He leaves a widow, three married daughters and a son, Dr. John Paton, practising in Orange.

ROY BRYANT MAYNARD.

DR. ROY BRYANT MAYNARD was born on February 5, 1905, at Bendigo. He was educated at Williamstown High School, and was a medical student at the University of Melbourne, graduating with honours in surgery and medicine. After periods as a resident medical officer at the Alfred Hospital and the Victorian Eye and Ear Hospital he became acting superintendent of the Victorian Eye and Ear Hospital, and also acted in the capacity of pathologist. For some years prior to his enlistment in the Australian Imperial Force he practised at Newport and continued as pathologist to the Victorian Eye and Ear Hospital. On his return from service, until he joined the full-time staff of the Repatriation Department, he was pathologist to the Victorian Eye and Ear Hospital and Central Hospital and consultant in Pathology to the Williamstown Hospital. Dr. Maynard died suddenly at his home on the morning of Thursday, March 10, 1960.

DR. E. J. GRIEVE writes: The sudden death of Roy Bryant Maynard has removed a man of substance from our midst. In his youth, Roy was a particularly smart sprinter, a good

all-round athlete and an excellent clubman. He had many interests and turned them to good account. A splendid collection of prints of sailing craft stemmed directly from his twin hobbies of yachting and photography, just as later on the urge to paint seemed to arise from the desire of a lifelong dog fancier to remember on canvas some of his favourite Gordon setters and boxers. We, for our part, will be happy to treasure in our hearts the memory of a dedicated, compassionate friend of humanity. To his wife, son and daughter we extend our very sincere sympathy on the loss of such a husband and father.

DR. A. P. DERHAM writes: I first knew Roy Bryant Maynard well when he became Commander of "A" Company of the 2/9 Australian Field Ambulance as a major on its formation in July, 1940, as part of the medical service of the Eighth Australian Division. In this capacity he trained his men first at Seymour and Puckapunyal and later at Bonegilla in northern Victoria, and went overseas with them on the *Queen Mary* to Malaya, together with other medical units of the Division.

When the Division came into full training later in the year, the companies took up their normal field function of forming advanced dressing stations to serve the troops in the manœuvres and later in action. In these tasks Major Roy Maynard displayed his usual intelligence and initiative, and one was always sure of his wholehearted cooperation. This was especially evident when the 27th Infantry Brigade Group arrived in August, 1941, carrying a moderate epidemic of mumps. A special camp hospital was established and Major Maynard was put in charge of it. He performed this task with enthusiasm and efficiency. Shortly afterwards Major Maynard, who had had considerable pathological experience before the war, was made assistant pathologist for the 2/10 Australian General Hospital, being also available for general duties, and from that time on Roy Maynard remained as pathologist to the 2/10 Australian General Hospital through the training period, the short campaign and three and a half years as a prisoner of war.

I did not see Roy again until after the war. I next came into professional contact with him at Rockingham Convalescent Home for ex-servicemen suffering war neuroses. This was in 1947 when I had a part-time appointment as visiting physician. Rockingham was administered as a ward of the Repatriation General Hospital, and all our pathological tests were referred to Roy Maynard's department there, which gave me the opportunity of discussing with Roy details of modern adult medicine—such, for instance, as liver function tests—and his help was tremendously valuable to me and to my patients. It was given freely, generously and without regard to the trouble involved to himself.

DR. G. F. S. DAVIES writes: My close association with Roy Maynard began in Malaya during World War II. This was in 1941, when Maynard was pathologist to the 10th Australian General Hospital which was already established. To me, as pathologist to the newly-arrived 13th Australian General Hospital, he gave invaluable help and advice. We spent some weeks together in Kuala Lumpur, where we attended the Malaria Research Laboratory of Dr. J. W. Field and were coached by him in the rapid diagnosis of malaria—a privilege which we both appreciated very highly. After this each returned to his unit, and soon the battle for Malaya began.

When this phase of the war had ended, we found ourselves working together in the Combined A.G.H. Laboratory at Changi. Here Maynard's resourcefulness bore fruit, and despite serious shortages of materials, the laboratory performed a useful function throughout the period of captivity.

Some years after the war our association was renewed. By this time Roy Maynard was Senior Specialist (Pathology) at the Repatriation General Hospital, Heidelberg. His time was divided between administration and morbid anatomy. He mastered the difficult art of cytological diagnosis of cancer cells, and this, in turn, contributed to the soundness of his opinion on histological sections.

Roy Maynard was a keen supporter of the College of Pathologists of Australia, and at a preliminary meeting in Tasmania strongly advocated the formation of a college rather than an association.

Roy Maynard's most endearing characteristic was his loyalty to his friends. I believe that no request to him for help was ever refused. Men of all ranks would go to him for help and advice on all kinds of personal problems, and they would go away comforted and usually with some practical plan of action. His family life was ideally happy and those who were privileged to enjoy his hospitality have the fondest memories of him in his family circle. Our deepest sympathy is extended to his wife and children.

DR. HEDLEY F. SUMMONS writes: I first met the late Dr. Maynard at the Victorian Eye and Ear Hospital in the middle 1930's; he was then part-time pathologist at the hospital and was also practising at Newport. He was a keen pathologist, being particularly interested in research on eye, ear, nose and throat diseases.

When I formed the 2/9th Field Ambulance, he became the Commander of "A" Company with the rank of Major. He trained with the unit in Australia, both at Seymour and at Bonegilla, and went to Malaya with the unit. Just prior to the outbreak of war in Malaya he was transferred, at the request of the Assistant Director of Medical Services, as pathologist to the 10th Australian General Hospital, and served with them during action. While a prisoner of war he served for three and a half years as pathologist of the Changi Hospital. After the war he returned as full-time pathologist to the Eye and Ear Hospital, and later was appointed pathologist to the Repatriation General Hospital, Heidelberg. During all the years that I have known him, I have found him at all times to be a very helpful and cooperative pathologist, and as an officer and doctor a very reliable and good friend.

SIR PETER MACCALLUM writes: Those of us who knew Roy Maynard as a friend begin, now that he is gone, to know how much that meant to us, and how sad and great a gap his going has left. When he was here, the hand was on the helm and the day was bright. We shall, I dare say, get used to his absence; but it will not be easy. His modesty, indeed diffidence, about his own worth, even as a student, might mislead his fellows; but they soon learnt it when they got to know him and realized his kindly, helpful competence and strength.

He came into his own as a soldier and as an administrator, great in both fields, but it was as a friend that he shone. Those he worked for—or better, those who worked under him—or those to whom unobtrusively he lent a hand can bear witness to the cheerful, friendly quality of their contact with him, his utter unselfishness and his readiness to help to the fullest of his power. And how great his power was, those will know who served and suffered (how severely we now realize) with him in Changi; so also those who have sat at his feet at the Repatriation General Hospital, Heidelberg, and gathered the fruit of his wisdom and counsel. It was ever a happy association, of which every member of his contented staff will have pleasant memories. They knew he was a friend. He never let anyone down.

Consequently and inevitably, the pathology laboratory under his influence became, as it should be, the hub of the hospital's interest. The Australian Repatriation Department has great reason to be thankful for his ambitious foresight and wise advice, and his constant watch over its function and the personal welfare of its officers. So, too, have the servicemen whose battles he fought, in season and out of season. So, too, has the College of Pathologists of Australia, on whose Council he also sat.

His realization of the importance of high-grade technical assistance made him a stimulating and admirable guide as chairman of the Examining Council (Victoria) of the Australasian Institute of Medical Laboratory Technology.

The astonishing quality of his senior laboratory departments and staff is yet another evidence of his success as a leader and director of laboratory services. It is no wonder that his laboratory was the first to qualify in Australia for recognition by the National Association of Testing Authorities as complying with their exacting standards. He built up the pathology services and equipment and the research activities to a standard that is second to none in Australia, and maintained a record system that is an outstanding example to its hospitals and a great credit to the department he so ably served. We can only hope it will not fall from its proud position now he is gone.

He was one of those people who seem to be irreplaceable. We may be forgiven for feeling, erroneously of course, that with his passing, the bottom has dropped out of everything. We have never had a better friend or a sounder leader than Roy Maynard. Our hearts go out to his family, with whom we share a grievous loss.

DR. W. E. E. LANGFORD writes: Dr. Maynard commenced duty with the Victorian Branch of the Repatriation Department in January, 1947, having been appointed to the position of Pathologist at the 115th Military Hospital, which was at that time being taken over from the Army by the Repatriation Commission, and which later became known as the Repatriation General Hospital, Heidelberg. In July, 1950, Dr. Maynard was appointed Senior Pathologist to the Victorian Branch, when, as well as being responsible for

the organization of a pathological service for the needs of the Victorian Branch of the Repatriation Department, he had included in his duties the role of part-time consultant to the Central Office of the Department, with the added responsibility of advising the Principal Medical Officer on the requirements of the department in the field of pathology for all the Branches of the Commonwealth.

Dr. Maynard "carried a torch" for his specialty. He was very much the idealist, so that he strove zealously for perfection in his objectives and resisted strongly any alternatives which he thought were not in the interest of pathology or of the Repatriation Department. He constantly sought improvements in the standards of the departmental service of which he was the leader, and was untiring in his efforts to obtain better accommodation, better equipment and better conditions for his staff. Within the limitations imposed by departmental budgeting, Dr. Maynard was sufficiently successful in his efforts to lay the foundations of a service which has met the needs of the Repatriation Department in a very efficient manner. Dr. Maynard's sudden death on March 10, 1960, at the age of 55 years deprived the Repatriation Department of one of its most valued medical officers. He had endeared himself to the staff, both lay and medical. As his Principal Medical Officer I miss him both as an adviser and as a friend.

Correspondence.

THE MANAGEMENT OF EARLY BREAST CANCER.

SIR: In the above-titled paper in your issue of May 21, 1960, it was the intention of the authors to set out a policy of treatment for breast cancer practised at the Peter MacCallum Clinic. This policy followed staff discussions, and it is not surprising that several letters which followed in your columns should criticize and disagree with our policy.

The main disagreement appears to emanate from the adherents of the simple mastectomy school. Our disapproval of simple mastectomy for potentially curable breast cancer rests on the belief that it is of the utmost importance to offer the maximum chance of complete cure to the individual patient who is fortunate enough to have limited axillary invasion. We wish to repeat that the choice of simple mastectomy for such a patient may well determine her death.

The logical prerequisite in our policy is, of course, careful selection of cases for the radical operation. Nevertheless, limitation of the field of usefulness of an operation cannot be regarded as failure of that operation. Thus McWhirter's figures for Stages I and II combined, of 58% five-year survivals are to be compared with Haagensen's figures of 66·6% five-year survivals in his personal series treated by radical mastectomy. Haagensen's selection of cases will undoubtedly have improved his figures; but his neglect of X-ray therapy (upon which McWhirter leans so heavily) certainly deprives him of even better survival figures.

We are criticized for considering radiotherapy as the definitive procedure for the internal mammary region, but not for the axilla. One important difference here arises from the fact that with kilovoltage equipment we have not been able to deliver with safety as high a dose to the axilla as the two-field arrangement permits in the internal mammary zone. Reasonable accessibility applies more to surgery than radiotherapy in one situation, and the reverse in the other.

All radiotherapists agree that mammary carcinoma is only a moderately radiosensitive tumour. We have noted repeatedly that invaded nodes after irradiation remain quiescent for only nine to twenty-four months and then reactivate in growth. This observation applies to unoperated areas and not "scarred axillæ" and applies to dosages higher than those advocated in Edinburgh.

Thus, our method of thinking suggests that a patient after radical mastectomy may already be cured. She would, in our opinion, only benefit from post-operative therapy if there are limited and radiosensitive metastatic deposits in the draining node areas. We do not believe that supraclavicular and mediastinal dissection could save a higher proportion.

The other point we wish to refer to is the question of lymphœdema of the arm following the radical operation. In a personal series of 100 cases (T.H.A.), there were nine cases with œdema of sufficient extent to trouble the patient. Several others, mostly obese subjects, had some œdema of the upper arm which caused no inconvenience. We feel that a relationship exists between late arm œdema and the occurrence of skin sloughing, wound infection and hæmatoma formation in the axilla. The free use of skin grafting and wound suction to prevent local fluid collections does much to achieve primary healing. Since excised lymphatics reform and anastomotic channels open only when local conditions are favourable, the employment of these methods lessens the likelihood both of lymphœdema and restricted arm movements.

With regard to the added effects of radiotherapy, measurement of the arm in cases following radical mastectomy and radiotherapy shows an increase of up to three-quarters of an inch circumference in the mastectomy arm in approximately one third of cases, and between one inch and two inches in a similar proportion. The former group is brought to light by measurement only and is not noticeable clinically. The latter group is noticeable clinically, but in the vast majority causes little or no discomfort. In the last four years we have searched for patients with marked lymphœdema complaining of symptoms for a trial of a new drainage operation. Of approximately 2500 patients with breast carcinoma passing through our clinics in that period, we found only eight of a degree meriting a description of marked œdema.

Finally, our reason for advocating post-operative X-ray therapy in Stage I outer quadrant tumours is that approximately 30% of these patients die of recurrence in spite of mastectomy and therefore must have metastasized either by the lymphatics or the blood-stream. We believe that this justifies a four weeks' treatment to the draining gland areas in this type of case. We have not yet seen a patient who has refused such treatment, even when its advantage was quoted as a possible additional 5% likelihood of cure. Obviously in the aged or weak such treatment is not even suggested to the patient.

Yours, etc.,

T. H. ACKLAND, M.D., M.S., F.R.C.S.,
W. P. HOLMAN, F.R.A.C.P., F.F.R.,
B. A. STOLL, M.R.C.S., F.F.R.

Peter MacCallum Clinic,
481 Little Lonsdale Street,
Melbourne.

August 2, 1960.

OTITIS MEDIA AND EXTERNA.

SIR: In reply to your correspondent I will endeavour to clarify the points which he raised.

1. Causative organisms in acute otitis media were not listed in their order of frequency of occurrence, as the decreased availability of pus for swabs, following the wide use of antibiotics in recent years, has made it virtually impossible to be dogmatic in many cases either regarding the identity of the causative organism, whether the patient would have recovered without an antibiotic, or whether the antibiotic was responsible for the infection subsiding without discharging and without the necessity for myringotomy.

2. One of my specialist informants was of the opinion that cases of residual hearing loss following acute otitis media are not infrequently seen by otologists.

3. In the treatment of otitis externa circumscripta, antibiotic therapy is indicated predominantly by the severity of the pain and the fact that early relief is urgent. I agree that the modern trend in the treatment of acute localized infections of the skin is to swing away from antibiotic therapy. However, the furuncle on the arm or leg is usually a much less distressing and less incapacitating condition than one in the external auditory meatus. In the absence of severe pain, I entirely agree that antibiotic therapy should rarely be necessary.

4. The taking of swabs for culture and sensitivity tests in the case of furuncle would depend upon whether antibiotic therapy was contemplated and, of course, upon whether pus was available. The emphasis on culture and sensitivity tests in cases of otitis externa diffusa rests upon two main facts. Firstly, some discharge is usually available and, secondly, a varied assortment of organisms may be responsible.

5. The recommendation of chloramphenicol or one of the tetracyclines for otitis externa circumscripta is based on the fact that the organism is usually a staphylococcus and at least two-thirds of the strains encountered in general practice are resistant to penicillin. This finding is based on the report of "Staphylococcal Infections of the Skin and

Subcutaneous Tissues in General Practice in Australia" (Johnson, Rountree *et alii*, 1960).

6. The presence, in very rare instances, of the tubercle bacillus in chronic suppurative otitis media was mentioned by a well-known specialist during personal correspondence on the subject. The comment was merely included for the sake of completeness.

14 Hobart Avenue,
Forrest,
Canberra, A.C.T.
August 1, 1960.

Yours, etc.,
ALEX JOHNSON.

ENUMERATION AND SIZING OF BLOOD CELLS BY MEANS OF ELECTRICAL GATING.

SIR: I read with interest the article by Douglas and Atkinson in the Journal of July 23, 1960, giving an account of their experience with the "Coulter Counter". It seems that the striking asymmetry of the cell size/population curves obtained with the machine led them to discover an error in the method prescribed by the makers for sizing red blood cells. However, correction of this error still leaves an asymmetry (their Figure V) unaccountable. The skewness is expressed as accounted for by 6526 cells, which is equivalent to 11·8% of the total cells.

The authors state that while Price-Jones curves have cell diameter as one coordinate, their own curves have cell volume against population, and they point out that this explains the relatively wide volume distribution of their curves.

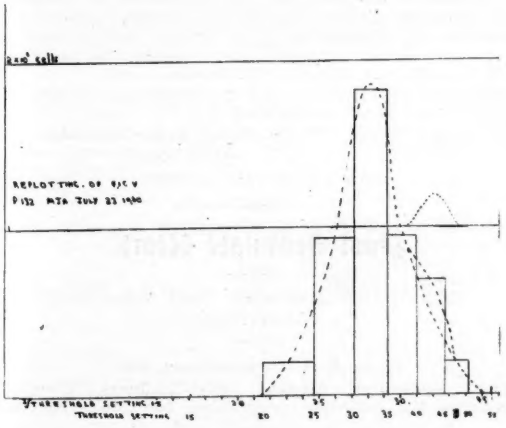

FIGURE I.
Replotting of Figure V of Douglas and Atkinson (see text).

This difference also explains a large measure of the residual asymmetry. If their Figure V is replotted with a contracting cube root scale on the "threshold setting" coordinate (so that the ordinate is proportional to the cube root of the threshold setting and hence to the cube root of the volume and hence to the diameter of the cells), then the density distribution curve is very nearly symmetrical. The skewness is now represented by 3% of the area enclosed by the curve, and is seen to be due to a restricted asymmetry occurring between the threshold settings 28 and 38, rather than to a true skewness. If the abscissa of the hump is plotted separately, it will be found to give a small symmetrical curve lying entirely between the threshold settings of 27·3 and 32·4 and having a median at about 32·5.

This lesser symmetrical curve must represent an additional symmetrical population passing through the electric gate. It is too large to be white cells, and out of place for doublets unless the assumption is wrong that doublets have a simple additive effect. The authors do not state the actual proportion of doublets; but as the correction used is about 10% of the machine count, doublets should produce a hump of the same order of magnitude centred about the threshold setting of 45, and this is not in evidence.

The accurate symmetry of the curves obtained in this way on the cube root contracting scale is evidence in favour of these two propositions: (i) Doublets do not have a simple additive effect in the electrical gate. (ii) Even in normal red cells the volume is proportional to the cube of the diameter.

Of more importance to the clinician is the fact that this replotting will enable the pathologist using the "Coulter Counter" to produce reliable Price-Jones curves. These are probably more informative than the mean corpuscular volume, but very expensive when produced by standard methods. If Figure VI is replotted with the new scale, the curve produced is again compounded of a major curve and a minor curve, the latter not involving the apex or the tail of the former. The hump is easily delineated by eye, and the major curve is seen to have the skew to the right, which was anticipated in this patient. The minor curve when plotted separately has the same relation to the major as is seen in the replotted Figure V (normal blood), which is further evidence for the effect being due to doublets. It might be possible, although hardly necessary, to eliminate the minor curve mathematically.

Maydena,
Tasmania.
July 27, 1960.

Yours, etc.,
M. D. GROUNDS.

A REPORT ON 500 CASES OF BLEEDING PEPTIC ULCER TREATED MEDICALLY WITH MINIMAL TRANSFUSION OF BLOOD.

SIR: We wish to reply to the points raised by Dr. F. J. Gray in your issue of July 23 in the following terms: (i) case selection; (ii) diagnostic criteria; (iii) thrombosis.

The article deals with "500 consecutive cases" of bleeding peptic ulcer, and the only case selection involved was the omission of cases where bleeding was considered to be due to a lesion other than peptic ulcer. The diagnosis of the cause of bleeding in cases that recovered was necessarily made according to the usual clinical criteria, and no doubt was subject to the possibility of a small percentage of error; the authors know of no certain method of diagnosis of peptic ulcer short of autopsy examination.

However, in regard to the cases of gastro-intestinal bleeding where death occurred, no death was attributed to a cause other than peptic ulcer except on autopsy evidence, and no case where bleeding from a peptic ulcer was found to have occurred during the terminal illness was excluded from the series; it was considered, however, that in four out of 10 such cases the bleeding was a minor factor in causing death (see article, under "Mortality"); in none of these four cases was vascular thrombosis the cause of death.

Morbidity: The statement of morbidity in the article is a complete one.

Indications for transfusion: If serial hæmoglobin estimations are done and the volume of blood in a recurrent hæmorrhage can be measured or estimated, then in some cases it is possible to deduce reduction of the hæmoglobin value below 3 to 4 grammes per 100 ml. The indications suggested for transfusion were stated to be "in general terms', and it is not suggested that the decision in the individual case was always easy or clear-cut.

Fluid balance: Fluid balance was maintained by the oral route in all but the occasional case.

Yours, etc.,
W. K. MANNING,
KEVIN O'CONNOR.

Repatriation General Hospital,
Concord.
New South Wales.
July 29, 1960.

THE ADMINISTRATION OF HALOTHANE VAPOUR MEASURED BY A ROTAMETER.

SIR: Since the publication of the paper with this title in THE MEDICAL JOURNAL OF AUSTRALIA for September 19, 1959, an improved version of the vaporizer has been made (see Figure I). The improvements incorporated in the new design are: (i) Greater compactness. (ii) The use of a polyethylene washer (which is resistant to halothane) between the bottle and the metal cap. (iii) The opening in the oxygen inlet tube has been reduced to one sixteenth of an inch, thereby giving the entering oxygen greater velocity

and increasing the maximum vaporization from 23 to 27·5 ml. per hour. (iv) Because of this greater vaporization, the oxygen inlet tube has been made shorter, allowing 25 ml. of halothane to be placed into the bottle instead of 15 ml. (v) In the earlier vaporizers, screwing the bottle into the

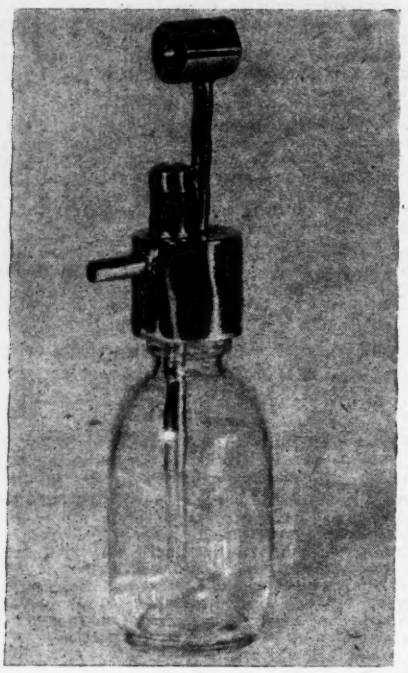

FIGURE I.

unyielding metal cap tended at times to break the bottle. This tendency has been enormously lessened in the most recently made vaporizers by grinding the bottle to fit the cap with automobile valve-grinding compound (3s. 3d. per tin at any garage).

342 Albert Street,
East Melbourne.
July 20, 1960.

Yours, etc.,
W. H. J. COLE.

Public Health.

POLICE OFFENCES (AMENDMENT) ACT, 1908, AS AMENDED, OF NEW SOUTH WALES.

THE Under Secretary, Chief Secretary's Department of New South Wales, has requested that publicity be given to the following proclamation, which was gazetted on August 5, 1960, applying Part VI of the *Police Offences (Amendment) Act* to phenazocine and certain other drugs. The proclamation will come into effect on February 6, 1961.

PROCLAMATION.

(L.S.)

E. E. WOODWARD.

Governor.

I, Lieutenant-General Sir Eric Winslow Woodward, Governor of the State of New South Wales, with the advice of the Executive Council, do, by this my Proclamation, declare that Part VI of the Police Offences (Amendment) Act, 1908, as amended, shall apply to:

Phenazocine (1, 2, 3, 4, 5, 6-hexahydro-8-hydroxy-6, 11-dimethyl-3-phenethyl-2, 6-methano-3-benzazocine) or (2′-hydroxy-5, 9-dimethyl-2-phenethyl-6, 7-benzomorphan), also known as NIH 7519, its salts, and any preparation, admixture, extract or other substance containing phenazocine,

Allylprodine (3-allyl-1-methyl-4-phenyl-4-propionoxypiperidine), its salts, and any preparation, admixture, extract or other substance containing allylprodine,

Benzethidine (1-(2-benzyloxyethyl)-4-phenylpiperidine-4-carboxylic acid ethyl ester), its salts, and any preparation, admixture, extract or other substance containing benzethidine,

Furethidine (1-(2-tetrahydrofurfuryloxyethyl)-4-phenylpiperidine-4-carboxylic acid ethyl ester), its salts, and any preparation, admixture, extract or other substance containing furethidine,

Levophenacylmorphan ((-)-3-hydroxy-N-phenacylmorphinan), its salts, and any preparation, admixture, extract or other substance containing levophenacylmorphan,

Metazocine (1, 2, 3, 4, 5, 6-hexahydro-8-hydroxy-3, 6, 11-trimethyl-2, 6-methano-3-benzazocine) or (2′-hydroxy-2, 5,9-trimethyl-6, 7-benzomorphan), its salts, and any preparation, admixture, extract or other substance containing metazocine,

Norlevorphanol ((-)-3-hydroxymorphinan), its salts, and any preparation, admixture, extract or other substance containing norlevorphanol,

Piminodine (1-(3-phenylaminopropyl)-4-phenylpiperidine-4-carboxylic acid ethyl ester), its salts, and any preparation, admixture, extract or other substance containing piminodine,

Norcodeine (N-demethylated codeine), its salts, and any preparation, admixture, extract or other substance containing not less than one percentum of norcodeine,

in the same manner as it applies to the drugs mentioned in paragraph (a) of subsection (2) of Section 18 of the said Act.

I hereby declare that this my Proclamation shall take effect on and from Monday, 6th February, 1961.

SIGNED and SEALED this twentieth day of July, one thousand nine hundred and sixty.

By His Excellency's Command,
C. A. KELLY.

GOD SAVE THE QUEEN!

Post-Graduate Work.

MELBOURNE MEDICAL POST-GRADUATE COMMITTEE.

PROGRAMME FOR SEPTEMBER, 1960.

THE Melbourne Medical Post-Graduate Committee announces the following programme for September, 1960.

Country Courses.

Mildura.—On September 17 and 18, in the Lecture Room, Nurses Home, Mildura Base Hospital, the following course will be given: Saturday, September 17: 2.15 p.m., "Management of Cardiac Infarction", Dr. A. Goble; 4 p.m., "Anæsthesia and Analgesia in Obstetric Practice", Dr. K. McCaul. Sunday, September 18: 10 a.m., "Problem Injuries of the Fingers", Mr. B. K. Rank; 11 a.m., quiz session. Dr. E. Broadbent, Mildura Base Hospital, is the local secretary. The fee for the course is at the rate of 15s. per session, but those who have paid an annual subscription to the Committee are invited without further charge.

Flinders Naval Depot.

On September 14, at Flinders Naval Depot, at 2.30 p.m., Dr. T. H. Hurley will lecture on "Some Advances in Hæmatology". This lecture is given by arrangement with the Royal Australian Navy.

Overseas Visitors.

Professor Georges Portmann, Honorary Dean of the Medical School of Bordeaux and the Senior Vice-President of the French Senate, will lecture at 5.15 p.m. on Monday, September 5, in the Wood Jones Lecture Theatre, University of Melbourne, on "The Surgical Treatment of Cancer of the Larynx". All medical graduates are invited to attend, without fee.

Professor A. G. R. Lowdon, Department of Surgery, University of Durham, Newcastle-upon-Tyne, will visit Melbourne for the week September 10 to 17. He will lecture

in the Medical Society Hall at 8.15 p.m., on Thursday, September 15, on "Acute Ischæmia of Limbs".

Professor Howard Taylor, of Columbia University, New York, will visit the Department of Obstetrics and Gynæcology, University of Melbourne, for one month from September 11. All medical practitioners are invited, without charge, to the following: obstetrics ward rounds, in Ward 18, Royal Women's Hospital, at 1 p.m. on Tuesday, September 13, 20 and 27 and October 4; lectures in the Pathology Lecture Theatre, Royal Women's Hospital at 1 p.m., as follows: Thursday, September 15, "Preeclampsia"; Friday, September 16, "Ante-Partum Hæmorrhage"; Thursday, September 22, "Abortion"; Friday, September 23, "Clinical and Pathological Studies of Carcinoma of the Ovary"; Thursday, September 29, "Endocrine Therapy in Obstetrics and Gynæcology"; Friday, September 30, "Graduate Education in Obstetrics and Gynæcology in the United States".

INFORMATION.

The address of the Melbourne Medical Post-Graduate Committee is 394 Albert Street, East Melbourne. Telephone: FB 2547.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Post-Graduate Training Fellowship in Psychiatry.

THE Senate of the University of Sydney has awarded a post-graduate training fellowship in psychiatry to Dr. Roger George Congdon, of Potts Point, New South Wales.

SEMINARS AT SYDNEY HOSPITAL.

THE following seminars will be held at Sydney Hospital during September and October, 1960.

September 7: "Surgery of Portal Hypertension", Mr. Norman Tanner, Consulting Surgeon to Charing Cross Hospital, London.

September 14: "Pituitary Disorders—Recent Advances in Diagnosis and Management", Dr. Peter Kendall, Endocrine Clinic.

September 21: No seminar—Sydney Hospitallers' Week.

September 28: "Acute Abdomen in the Newborn Infant", Dr. E. Rohan Williams, Director of the Radiological Department, St. Mary's Hospital, London.

October 5: "Reflections on Inflammation and its Experimental Investigation", Professor D. L. Wilhelm, Professor of Pathology, University of N.S.W.

October 12: "Coronary Angiography", Dr. George Michell (by invitation), Cardio-Vascular Clinic.

October 19: "Experimental Investigations on Diabetes Mellitus", Professor F. G. Young, Professor of Biochemistry, University of Cambridge.

October 26: "The Place of Surgery in Peptic Ulceration", Mr. Peter H. Greenwell, Gastro-Enterology Clinic.

These seminars will be held on Wednesday from 2 to 3 p.m. in the Maitland Lecture Theatre. They will be preceded by medical grand rounds at 12 noon and by a pathological demonstration ("Organ Recital"), at 1.30 p.m.

ST. VINCENT'S HOSPITAL, SYDNEY: GASTRO-ENTEROLOGY UNIT.

A MEETING of the Gastro-Enterology Unit of St. Vincent's Hospital, Sydney, will be held on Thursday, August 25, 1960, at 5.30 p.m. Dr. Bruce Hall will speak on "Ulcerative Colitis". All medical practitioners are invited to attend.

SEMINAR AT THE ROYAL NORTH SHORE HOSPITAL OF SYDNEY.

THE monthly seminar at the Royal North Shore Hospital on September 6, 1960, will be given by Dr. Zelman Freeman, whose subject will be "The Vector Approach to Standard Electrocardiography".

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JULY 16, 1960.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	..	..	6(4)	..	..	..	..	..	6
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	2	..	9	..	..	..	4	..	15
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	..	26(24)	6(5)	..	2(2)	..	7	3	44
Diphtheria	..	..	..	..	..	..	..	..	..
Dysentery (Bacillary)	..	1(1)	..	6	..	..	3	..	10
Encephalitis	..	..	..	1(1)	..	..	..	..	1
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	53(20)	35(30)	4(1)	22(15)	7(4)	..	..	..	121
Lead Poisoning	..	..	1	..	..	..	..	..	1
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	2(1)	..	..	..	..	..	2
Malaria	..	..	1(1)	..	..	..	1	..	2
Meningococcal Infection	2	2	..	..	..	..	..	..	4
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	..	2(2)	..	2(2)	..	..	..	..	4
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	..	6(5)	..	..	2(2)	..	..	..	8
Salmonella Infection	..	..	..	..	2(2)	..	..	..	2
Scarlet Fever	10(4)	14(8)	4(3)	..	..	4	..	..	32
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	2(2)	..	..	..	..	..	2
Trachoma	..	..	..	..	1	..	..	..	1
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	33(19)	16(12)	9	..	5(2)	..	2	..	65
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

The Royal Australasian College of Physicians.

EXAMINATION FOR MEMBERSHIP, 1961.

AN examination for membership of The Royal Australasian College of Physicians will be held on the following dates: Written examination: capital cities, Friday, March 10, 1961. Clinical examination: Sydney, commencing on or about Wednesday, April 19, 1961; Perth, Wednesday, April 26, 1961. Applications must be lodged by Friday, February 10, 1961.

Applications to appear before the Board of Censors should be made in the prescribed form, and must be in the hands of the Honorary Secretary of the College before the closing date advertised. Candidates should signify in which city they desire to take the written examination. Only those candidates whose answers in the written examination have attained a satisfactory standard will be allowed to proceed to the clinical examination. Application forms are obtainable from the Honorary Secretary, 145 Macquarie Street, Sydney.

The clinical examination will be held in Sydney; but if sufficient candidates are offering for examination in Perth, a clinical examination will also be held in Perth on or about Wednesday, April 26, 1961. Intending candidates are asked to state on their applications where they would desire to take the clinical examination.

Corrigendum.

MUSCULAR EFFORT AND POSTURE IN HIATUS HERNIA.

IN the article on "Muscular Effort and Posture in Hiatus Hernia', by C. Craig in our issue of July 30, 1960, on page 178, column 2, paragraph 3, line 10 should read ". . . left anterior oblique position" instead of ". . . left occipito-anterior position". We regret this error.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Selecki, Edward Emanuel, M.D., 1951 (Univ. Cracow), Regional Section, 17 (2A), Royal Newcastle Hospital, Newcastle.

Satrapinsky, Zoya, M.B., B.S., 1959 (Univ. Sydney), 59 Courallie Avenue, Homebush West.

The undermentioned have been elected as members of the New South Wales Branch of the British Medical Association: Jervie, Ann Elizabeth, M.B., B.S., 1960 (Univ. Sydney); Yip, Edwin Pak Wah, M.B., B.S., 1960 (Univ. Sydney); Hooper, Nanette Catherine Mary, M.B., B.S., 1959 (Univ. Sydney); Haskins, Jan Margaret, M.B., B.S., 1959 (Univ. Sydney); Peak, Howard John, M.B., B.S., 1959 (Univ. Sydney); Satrapinsky, Zoya, M.B., B.S., 1959 (Univ. Sydney); Wright, George Henry, M.B., B.S., 1959 (Univ. Sydney); Brieger, Hans Hillel, M.D., 1923 (Univ. Breslau), Reg. Section 17 (2A); Nagy, Laszlo, M.D., 1944 (Univ. Budapest), licensed under Section 21c (4) of the *Medical Practitioners Act* 1938-1958; Nathan, Henry, licensed under Section 21 of the *Medical Practitioners Act*, 1938-1958, for post-graduate research at the Royal North Shore Hospital.

Deaths.

THE following deaths have been announced:

SAPSFORD.—Clinton Pelham Sapsford, on August 9, 1960, at Brisbane.

LITTLEJOHN.—Charles William Berry Littlejohn, on August 4, 1960, at Melbourne.

MCLEAN.—Kenneth Arthur McLean, on August 8, 1960, at Melbourne.

SANDER.—Ralph Sander, on August 10, 1960, in Kent, England.

Diary for the Month.

AUGUST 23.—New South Wales Branch, B.M.A.: Hospitals Committee.
AUGUST 23.—Tasmanian Branch, B.M.A.: Southern Subdivision.
AUGUST 24.—Victorian Branch, B.M.A.: Branch Council.
AUGUST 25.—Tasmanian Branch, B.M.A.: Northern Subdivision.
AUGUST 25.—New South Wales Branch, B.M.A.: Clinical Meeting.
AUGUST 26.—Queensland Branch, B.M.A.: Council Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned; or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

Authors of papers are asked to state for inclusion in the title their principal qualifications as well as their relevant appointment and/or the unit, hospital or department from which the paper comes.

References to articles and books should be carefully checked. In a reference to an article in a journal the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of article. In a reference to a book the following information should be given: surname of author, initials of author, year of publication, full title of book, publisher, place of publication, page number (where relevant). The abbreviations used for the titles of journals are those of the list known as "World Medical Periodicals" (published by the World Medical Association). If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors submitting illustrations are asked, if possible, to provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary is stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this Journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in Australia can become subscribers to the Journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £6 *per annum* within Australia and the British Commonwealth of Nations, and £7 10s. *per annum* within America and foreign countries, payable in advance.